Presentation on the International Understanding of, and Response to, Risk of Hepatitis and HIV/AIDS

Introduction

1. This presentation seeks to examine the international perspective, focusing on a sample of countries. It begins with consideration of the extent of self-sufficiency and the use of factor concentrates, both locally produced and imported, in various countries. It goes on to look at aspects of the developing international understanding of the risk of hepatitis, with additional information relating to specific countries. The presentation then considers aspects of the developing international understanding of the risk of HIV/AIDS. These parts of the presentation regarding knowledge of risk of hepatitis/HIV/AIDS should be considered in conjunction with the Inquiry's more detailed Knowledge of Risk Chronology [INQY0000006] and presentation of the chronology [INQY1000056] and [INQY1000057]. A section follows referring to some material concerning the particular understanding of the risk of HIV/AIDS in a sample of countries. In relation to each country, consideration is then given to the responses made within the country and any statistics that are available on the infection rates. Finally, the presentation addresses the developing understanding of hepatitis C and the particular circumstances of a sample of countries, their responses to the developing knowledge and any statistics that are available in relation to infection rates.

2. This presentation is, by necessity, broad brush, and seeks to highlight some of the key events particularly in Europe, so that events in the United Kingdom can be seen, to some extent at least, within an international context. The presentation is inevitably selective in relation to the countries that are considered. It is important to point out that there are considerable limitations arising from the availability and accessibility of documents from, or relating to, other countries. This does not, therefore, purport to be a comprehensive

account, either in relation to the individual countries considered or in relation to the international picture in general.

3. This presentation does not address events in Canada or Ireland, where there have, of course, been public inquiries (the Krever Inquiry in Canada[1] and the Lindsay Tribunal and the Finlay Tribunal in Ireland[2]), and so a detailed consideration of what happened in those countries is already in the public domain.[3]

Self-sufficiency and use of factor concentrates

Netherlands

4. From 1961, blood collection in the Netherlands was undertaken exclusively through the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service ("CLB"), a division of the Netherlands Red Cross. The Human Blood Act 1961 mandated that self-sufficiency should be achieved in the Netherlands.[4]

5. In addition to collecting blood and plasma, the CLB manufactured Factor VIII and IX concentrates which were then distributed throughout the Netherlands. The CLB was the only fractionation laboratory in the Netherlands.[5]

6. Regional blood banks also collected blood and produced cryoprecipitate with surplus plasma being provided to the CLB.[6] All blood was collected on a voluntary, unpaid basis. Hospital blood banks operated until 1985, but were being gradually phased out from 1974 and replaced with regional blood banks.[7]

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[1] KREV0000001.

[2] HSOC0020469; DHSC0015673. See also the Institute of Medicine report relating to the USA: JREE0000019.

[3] The Inquiry has also received written [WITN7418001 and WITN7418016] and oral evidence from Mr O'Mahony about Ireland's response to contaminated blood.

[4] CBLA0000058_036 at p.7.

[5] CBLA0000058_036 at p.4.

[6] For detailed evidence received by this Inquiry in relation to Groningen, see WITN6412001.

[7] CBLA0000058_036 at pp.4 and 5.

[8] BAYP0000022_050 at p.9. Though a draft witness statement of Dr Van Aken suggests that this was

7. In 1972, the CLB was producing freeze-dried cryoprecipitate from four donors.[8] Dr van der Meer, Central Laboratory, Blood Transfusion Service, Amsterdam, had the view at that time that *"it is realistic to aim at increased production of cryoprecipitate in order to meet the demand for the first few years. Only a few centres should undertake to produce highly concentrated AHF products for treatment of patients with AHF inhibitors and for biochemical studies. Only when the production of cryoprecipitate has attained a satisfactory level one could start to produce high potency material on a large scale."*[9]

8. From 1975, the regional blood banks also produced wet (not freeze dried) cryoprecipitate for the regions they supplied.[10]

9. In addition, a number of foreign imported blood products were licensed and available for use in the Netherlands and it was a matter of choice for the physician and/or hospitals as to the products which would be used. It is unclear whether the CLB had any role in the importation of these products. One document suggests that foreign imported products were purchased directly from manufacturers by the hospitals;[11] another that the CLB bought the products and sold them on to the hospitals.[12] Initially only Baxter product was imported. However, after litigation concerned with unfair competition, Armour product was also imported.

10. However, Dr van Aken, Medical Director, CLB, suggested that there was limited take up of the imported factor concentrates because *"haemophilia physicians considered that [convenience and the benefits of home treatment] were less important than the achievement of self-sufficiency."*[13] However, in an article published in 1981, Sjamsoedin-Visser, of the University Children's Hospital in Utrecht, described the establishment of a home treatment programme in Bilthoven in 1974.[14] They state that *"In about 90% of transfusions we make use of cryoprecipitate of both*

commenced in 1987: CBLA0000058_036 at p.9.
[9] BAYP0000022_050 at p.9.
[10] CBLA0000058_036 at p.7.
[11] CBLA0000058_036 at p.5.
[12] CBLA0000058_036 at p.9.
[13] CBLA0000058_036 at p.7.
[14] RLIT0001956.

lyophilized and frozen products (small pools of 4 donors)'. They note that these were manufactured by the CLB or obtained from Dutch regional blood banks. Where allergic reactions occurred, *"If reactions occur more than sporadically we switch to dried Factor VIII concentrates'*. It is recorded that the CLB had started to manufacture Factor VIII concentrates *"this year"* i.e. 1981. The author *"investigated why only 30% of our patients are on HT. A large group of patients (15%) are reluctant to participate; also a number of physicians gave negative advice. In the Netherlands where distances are of little importance and intensity of care is high, HT may be not seem necessary by some physicians and patientsl*, but the article concluded that home treatment was beneficial and should be pursued.

11. Dr van Aken's witness statement, as well as some other documentation, provides the following information on pool sizes:

Product	**Pool size identified in various years**		
CLB Cryoprecipitate	1972 4 donors[15]	1985 2 donors[16]	1987 4 donors[17]
CLB Factor VIII Concentrate	1979 - 1986 700kg (2,800 donors)[18]	1986 - mid-1988 1,500kg (6,000 donors)[19]	1990 onwards Varies between 2,000L and 4,000L[20]
CLB Factor IX Concentrate	Until 1988 Varied between 400kg and 600kg[21]	Since 1988 Varies between 1,000 and	

[15] BAYP0000022_050 at p.9.
[16] LCAN0000018_101 at p.6.
[17] CBLA0000058_036 at p.7.
[18] CBLA0000058_036 at p.31.
[19] CBLA0000058_036 at p.31.
[20] CBLA0000058_036 at p.31.
[21] CBLA0000058_036 at p.31.
[22] CBLA0000058_036 at p.31.

		2,000kg[22]	

12. From 1980, the approach to treatment of haemophilia gradually changed; "*patients were treated with higher dosages of factor VIII and more patients were treated with concentrate instead of cryoprecipitate.*"[23] In addition, from 1981, the CLB manufactured Factor VIII concentrate (intermediate purity). From 1982 the amount of factor concentrate imported from the US dropped from a high of 7 million IU in 1982 to 3.5 million IU in 1984. Factor IX concentrate used in the Netherlands all came from the CLB, except for that used by the Groningen centre which imported Factor IX rather than use the CLB product.[24]

13. In a recent interview, Cees Smit, Coordinator of the Netherlands Haemophilia Society (NHVP) between 1987 and 1998, has said that in January 1983, in the light of the risks posed by use of American concentrates, physicians had agreed to use only cryoprecipitate in children under 4 years old and that cryoprecipitate was considered to be the treatment of choice for all other patients, followed by local (small pool) concentrate.[25] Advice to this effect was published on 27 February 1983.[26]

14. In April 1983, the Director General of the National Institute of Public Health and Environmental Protection wrote to the Minister of Health to explain that most experts agreed that US factor concentrates should not be used. He further explained that the use of imported Factor VIII concentrate made from plasma of paid donors should be prohibited until further notice but that physicians of people with haemophilia *"who had signed a consent were exempt"*.[27] However, that ban was not introduced: but it is understood that most physicians followed the agreement mentioned in paragraph 13.

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[22] CBLA0000058_036 at p.31.
[23] CBLA0000058_036 at p.9; PRSE0001143 at p.5.
[24] CBLA0000058_036 at p.10.
[25] JEVA0000180 **JEVA0000181**
[26] **WITN6411010**
[27] KREV0000001 at p.923.

15. In January 1985, the CLB started to develop heat treated cryoprecipitate and in February 1985, the CLB reduced the number of donors for their freeze-dried cryoprecipitate from four to two donors.[28]

16. In November or December 1985, the CLB introduced heat-treated cryoprecipitate.[29] The regional blood banks could only produce wet cryoprecipitate and did not have the funding or technology to produce heated products on a large scale. Consequently, over time their production decreased: between 1985 and 1989, the production of cryoprecipitate at the Dutch regional centres decreased from 11 million IU to 4.6 million IU.[30]

17. A report of the May 1986 Council of Europe Committee of Experts on Blood Transfusion and Immunohaematology, compiled on the basis of data provided by member states, recorded for the Netherlands that in terms of the treatment for people with haemophilia, between 98% and 99% of the country's Factor VIII was provided by way of cryoprecipitate. 7% of the Factor VIII concentrate and 1% of the Factor IX concentrate was provided by commercial companies. This did not identify the source of the plasma. [31]

18. In 1987, it appears that the CLB went back to producing lyophilised (i.e. freeze dried) cryoprecipitate from pools of 4 donations.[32]

19. On 1 January 1988, the Assistant-Minister of Health in the Netherlands ordered that only heated cryoprecipitate and heated Factor VIII concentrate were permitted for use.[33] The regional blood banks which still produced non-heat treated cryoprecipitate at that time ceased production of it.[34]

[28] LCAN0000018_101 at p.6.
[29] LCAN0000018_101 at pp.2 and 8.
[30] CBLA0000058_036 at p.8.
[31] PRSE0003860.
[32] CBLA0000058_036 at p.7.
[33] LCAN0000018_101 at p.8.
[34] LCAN0000018_101 at p.8.

20. In 1989, plasma was being imported (10,000 litres) but it appears to have only been from other EEC countries.[35] In terms of Factor VIII concentrate, 3 million IU was imported in 1989 from "outside Europe", compared to 3.5 million IU in 1986.[36]

21. In 1998, the CLB and regional centres merged to create a single not for profit organisation, 'Sanquin', responsible for the management of blood and blood products.[37]

Germany

22. In the Federal Republic of Germany, a variety of bodies were involved in the provision of blood and blood products, with governmental institutions, not for profit organisations and commercial companies dealing with blood products, and commercial companies, organisations such as the Red Cross, and blood transfusion centres at large hospitals operating the whole blood collection and distribution system.[38] The Krever report noted that 25% of Germany's blood and blood components were collected by 80 public blood banks but that most of the plasmapheresis was undertaken by commercial centres.[39] The principal regulator of blood and blood products through the 1980s was the federal government – the Federal Health Office (Bundesgesundheitsamt).[40]

23. In 1986, Council of Europe data indicated that there were approximately 6,000 people with haemophilia A or B in the Federal Republic of Germany.[41] It appears that treatment was split between 10% of treatment with cryoprecipitate and 90% with imported factor concentrate.[42] No data was provided in response to the Council of Europe's survey in 1989 detailing the usage of Factor VIII in 1989; it is recorded that the Federal Republic of Germany used 180 million IU in 1986.[43]

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[35] NHBT0010040_001 at p.17.
[36] NHBT0010040_001 at p.20.
[37] RLIT0001914.
[38] RLIT0000456 at p.207.
[39] KREV0000001 at p.851.
[40] KREV0000001 at p. 851.
[41] PRSE0003860 at p.9.
[42] PRSE0003860 at p.11.
[43] NHBT0010040_001 at p.26.

24. In 1984, Germany was not required to record the origin of plasma, and information about the size of the donor pool and donor selection was not recorded. The proposal for such a requirement had been actively rejected by pharmaceutical manufacturers, physicians and the Haemophilia Society.[44] In 1989, 90% of Factor VIII and Factor IX concentrate that was used within the Federal Republic was imported with no designation of the country of origin of the plasma.[45]

Belgium

25. A 1986 Council of Europe report states there were 850 people with haemophilia A and 150 people with haemophilia B in Belgium.[46] A report in 1989 gives somewhat different figures: 549 people with haemophilia in 1986 and 650 people in 1989.[47]

26. Dr Walford and Dr Gunson visited the Blood Transfusion Service in Leuven, Belgium in April 1981. They noted that Belgium had *"almost reached self-sufficiency"* with respect to Factor VIII concentrate *"by combining plasma separation from whole blood donations with plasmapheresis"*.[48] Donors were volunteers only.[49]

27. A Council of Europe report dated 1989 confirmed that Belgium was self-sufficient in Factor VIII and had been in 1986.[50] However, other data supplied to the Council of Europe in 1986 indicates that of the treatment given to people with haemophilia, 1% was imported Factor VIII and 1% was imported Factor IX with the remainder being cryoprecipitate. It is not clear which country the Factor VIII and IX concentrate originated from.[51]

28. A paper for the Working Party on Plasma Supply, tabled on 24 April 1981, indicates that in Belgium the Leuven centre produced frozen single cryoprecipitates whereas the

[44] RLIT0000456 at pp.215-216.
[45] PRSE0003860 at pp11-12..
[46] PRSE0003860 at p.9.
[47] NHBT0010040_001 at p.25.
[48] CBLA0000042_113 at p.1.
[49] CBLA0000042_113 at p.5. See also: draft witness statement of Dr van Aken, CBLA0000058_036 at p.32.
[50] NHBT0010040_001 at p.21.
[51] PRSE0003860 at p.11.

Brussels centre produced frozen pooled cryoprecipitate with a maximum pool size of 1,000 donations from the same centre.[52] The writer of the paper suggests that *"Large pools incur a larger number of exposures to e.g. HBV but offer better opportunities for quality control of homogenous batches. While the method of asceptic pooling .. is ingenious and the system incorporates conscientious quality control, it reflects attitudes to "good pharmaceutical manufacturing practice" some 5 years behind current regulatory thinking in the US or UK".* [53] It is unclear who the writer of the paper is.[54]

29. In their report in 1981, Dr Walford and Dr Gunson also noted that Factor VIII concentrate was available *"in adequate quantities ... due largely to the use of freeze-dried cryoprecipitate which comprises 85% of the total FVIIIC used"*. The remainder was intermediate concentrate.[55] By 1989, it was reported that 24 million IU large pool cryoprecipitate had been used and no other Factor VIII products.[56] The volume used had declined slightly, from 24.6 million IU, since 1986.[57]

Denmark

30. In 1977, the Ministry of the Interior established a blood products committee to examine the collection and distribution of blood and production of fractionated blood products. In its 1980 report, the committee noted WHO and other recommendations that the national blood service should be run using voluntary, unpaid donors and that the country should strive for self-sufficiency. While Denmark had a non-commercial blood transfusion service at that time, it was not self-sufficient because of the use of the Bonn protocol for inhibitors.[58]

31. In 1986, it was recorded that 70% of Factor VIII and 53% of Factor IX that was used for the treatment of patients with haemophilia was imported with the balance coming

[52] DHSC0002207_071 at p.3.
[53] DHSC0002207_071 at p.4.
[54] A handwritten note suggests it may have been Dr Jim Smith. The minutes of the meeting are at DHSC0002207_073.
[55] CBLA0000042_113 at p.1. See also DHSC0002207_071.
[56] NHBT0010040_001 at p.27.
[57] NHBT0010040_001 at p.26.
[58] RLIT0000456 at pp.178-179.

from Danish plasma.[59] A figure of 4.5% was given for use of cryoprecipitate but it is somewhat unclear what it is a percentage of.[60] It appears that the imported Factor VIII amounted to 18.5 million IU, with 4.6 million IU coming from the EEC and 13.9 million IU being imported from Council of Europe and "Others".[61]

32. In a Council of Europe report in 1989, it is recorded that Denmark imported no plasma but did import 8.0 x10^6 IU of Factor VIII from EEC and Council of Europe (non-EEC) countries. It imported no Factor VIII from outside of Europe.[62]

Finland

33. A 1991 article reported that the blood service had been run by the Finnish Red Cross since 1948 and that blood donation had always been voluntary and unremunerated, with self-sufficiency in both blood and plasma for blood products.[63]

34. It is thought that Finland ceased to take blood donations from prisoners by 1974 and it appears that this was *"to avoid transmission of hepatitis B virus but it was considered that there might be other, unknown viruses as well"*.[64]

35. In 1983 there were thought to be about 200 people with severe haemophilia and 270 with von Willebrand disease in Finland.[65]

36. *"More active use of fresh frozen plasma"* was used for the treatment of haemophilia A in 1957-1959, followed by the introduction of cryoprecipitate in 1967.[66] From 1969, *"adequate amounts of lyophilised cryoprecipitate made of 2-8 units of pooled plasma"* were available.[67] Most cryoprecipitate was prepared using an eight-donor method.[68] Use

[59] PRSE0003860 at pp.11-12.
[60] PRSE0003860 at p.11.
[61] NHBT0010040_001 at p.21.
[62] NHBT0010040_001 at p.17 and p.20.
[63] NHBT0000101_039 at p.15. See also NHBT0010040_001 and SBTS0000033_071 at p.2.
[64] PRSE0000179 at para 6.
[65] SBTS0000231_022 at p.15.
[66] DHSC0002341_005 at p.1.
[67] DHSC0002341_005 at p.1; SBTS0000231_022 at p.14.
[68] SBTS0000231_022 at p.14.

of lyophilised small pool cryoprecipitate continued between 1980 and 1984 because no other products were readily available.[69]

37. However, the Finnish Red Cross developed its own intermediate purity concentrate ("AHF 20") in 1982 and 1983 but this was only used for the home treatment of a small number of haemophilia A patients and hospitals continued to use cryoprecipitate.[70] No source has yet been found to verify the actual pool sizes used in production of AHF-20 but it has been described, by Ebeling, Rasi, Naukkarinen and Leikola in an article in the Annals of Medicine, as being a *"large pool concentrate"*.[71]

38. According to Dr Leikola, Director of the Finnish Red Cross Blood Transfusion Service, the policy of restricting the use of factor concentrates was instituted because of the potential risk of AIDS and hepatitis:

> *"Because of the known (since 1983) risk of AIDS from American commercial F VIII concentrates, the Finnish haemophiliacs were persuaded not to use imported products should they be introduced to the Finnish market. Commercial preparations of plasma-derived F VIII concentrate did not come to the Finnish market in the 1980's, with the exception of some special preparations for patients with strong F VIII inhibitors…. Since the risk of hepatitis and the potential risk of AIDS were recognised, AHF-20 was instructed to be used exclusively for home treatment. Hospitals were urged to continue using cryoprecipitate"*[72]

39. However, Dr Leikola also noted that although cryoprecipitate was the primary treatment, Finland did not regard it as superior to concentrate, rather it was recognised that *"Finland would not be able to cover all its need with voluntary finished plasma should there be an overall use of concentrate. Therefore partial use of cryoprecipitate was considered necessary also from that point of view."*[73]

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[69] PRSE0003241 at p.2; PRSE0004403 at p.1.
[70] Only 17 patients: PRSE0003241 at p.3.
[71] PRSE0004403 at p.3.
[72] PRSE0003241 at paras 10 and 11.
[73] CBLA0000066_004 at p.61.

40. A small amount of activated prothrombin complex was imported for patients with *"strong"* inhibitors, for one patient at a time.[74]

41. Finland was also in a position to export Factor VIII concentrate to Norway and Iceland until 1988, although the precise dates and time periods over which this took place are unclear.[75]

42. Between 28 and 31 May 1986 the Committee of Experts on Blood Transfusion and Immunohaematology held a conference in Berne ("the Berne conference"). An extract from their report dealing with AIDS sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[76] The information provided by Finland was as follows:

    a. In terms of the treatment of people with haemophilia, 50% of the country's Factor VIII was provided by way of cryoprecipitate.
    b. Finland was self-sufficient in concentrates.

Norway

43. Until 1982, lyophilised cryoprecipitate of Norwegian or Finnish origin was used to treat people with haemophilia A and von Willebrand's disease, with the exception of a nine month period between June 1980 and April 1981 when US factor concentrates were imported.[77] Approximately 55 Norwegian people with haemophilia received this product.[78] The Finnish product was supplied by the Finnish Red Cross.[79]

44. From 1975, haemophilia B patients were treated with Factor IX concentrates sourced from pools each collected from 250 donors.[80]

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[74] PRSE0003241 at p.3; CBLA0000016_032 at p.3.
[75] NHBT0004024_003 at p.3.
[76] PRSE0003860.
[77] RLIT0001245 at p.2.
[78] RLIT0001245 at p.4.
[79] RLIT0001245 at p.5.
[80] RLIT0000286 at p.3.

45. From 1982, Norway was self-sufficient with respect to clotting factor concentrates. Haemophilia A patients were treated with lyophilised cryoprecipitate, with each lyophilised bottle containing cryoprecipitate from 6 donors[81], or they were treated with single donor cryoprecipitate.[82] This was sourced from volunteer donors.[83]

46. By 1986 1-2% of the Factor VIII concentrate and 0% of the Factor IX concentrate was provided by commercial companies. This commercial product did not identify the source of the plasma on the label, but the information was given to the haemophilia centre.[84]

47. The use of cryoprecipitate dropped from nearly 20,000 units per million inhabitants in 1985 to about 11,000 in 1987, to nearly 0 in 1990.[85] The use of fresh frozen plasma for transfusion increased throughout this period, and by 1993 was replaced by plasma treated for viral inactivation with solvent detergent.[86]

48. As at 1986, cryoprecipitate (presumably freeze dried) was predominantly used to treat haemophilia patients (98-99%), and just 1-2% of total Factor VIII used came from imported concentrate. No imported Factor IX was used.[87] It is unclear why imported Factor VIII concentrate was used at all in 1986, given the other documentation that suggests that Norway was self-sufficient from 1982. A Council of Europe survey indicates that no plasma or Factor VIII concentrates were imported in 1989.[88]

49. In 1986, a pilot project for contract fractionation was initiated by the Red Cross and National Hospital Blood Centre.[89] Throughout 1987-1988 an increasing number of blood banks joined, and the Norwegian Plasma Fractionation Project was established in 1989 to take over the co-ordination of contract fractionation.[90] Plasma fractionation was performed abroad, by contract with Octapharma, but the plasma remained the property

[81] RLIT0001245 at p.4.
[82] NHBT0009083_009 at p.6. See also RLIT0001246 at p.1.
[83] RLIT0001245 at p.2.
[84] PRSE0003860.
[85] RLIT0001244 at p.5.
[86] RLIT0001244 at p.5.
[87] PRSE0003860 at p.12.
[88] NHBT0010040_001 at p.17 and p.20.
[89] RLIT0001244 at p.2.
[90] RLIT0001244 at p.2.

of the blood banks and the final products were returned to them. It is said, by Flesland, Seghatchian and Solheim in an article in Transfusion and Apheresis Science, that this initiative, together with the postponement of elective orthopaedic surgery in people with haemophilia and a special grant by the Norwegian Parliament for equipment for freezing and storage of plasma, *"enabled the transition to virally inactivated plasma products with the retention of self-sufficiency."*[91]

50. This transition is also apparent from the usage figures; the use of cryoprecipitate dropped from nearly 20,000 units per million inhabitants in 1985 to about 11,000 in 1987, to almost 0 in 1990.[92] However, the use of fresh frozen plasma for transfusion increased throughout this period.[93]

Iceland

51. In 1989, a Council of Europe Report stated that there were 70 haemophilia A patients in Iceland.[94] It was thought that there were approximately 14-16 patients with severe haemophilia A, with the remaining patients having mild haemophilia A.[95] A 2010 World Federation of Haemophilia Global Survey stated that, at that time, there were 64 people with haemophilia and 96 people with von Willebrand disease in Iceland, out of a population of 308,910.[96]

52. Blood banking in Iceland appears to have been limited in terms of staffing as well as having ongoing difficulties with the physical accommodation of the blood bank until 2007.[97] In a document, thought to be from 1977, it is noted that no legislation was in place regarding procurement of plasma and Iceland did not *"have any pharmacopoeial requirements for plasma products."*[98]

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[91] RLIT0001244 at p.2.
[92] RLIT0001244 at p.5.
[93] RLIT0001244 at p.5.
[94] NHBT0010040_001 at p.25 (no data was available in relation to 1986).
[95] RLIT0000470 at p.1.
[96] RLIT0000460 at p.17.
[97] RLIT0000462.
[98] SBTS0003019_002 at p.4.

53. Two documents state that Factor VIII was imported from Finland. The dates of the start of that importation differ – one indicating it was from 1973[99] and another from 1976.[100] Although it is recorded that in 1975 Iceland produced 160 litres of frozen plasma, there is no data on how the plasma was used. [101] No data has been identified delineating factor concentrate usage from cryoprecipitate use in the 1970s.

54. In 1985, there were moves to buy plasma from France because it was cheaper. However, Þórarins Ólafssonar, chief physician at Landspítalan's anesthesiology department, prevented the purchase taking place. Similarly, between 1970 and 1989 the Icelandic health authorities were offered cheap blood products from the USA but this was refused by Ólafur Jensson, the Blood Bank's chief physician. [102]

55. Data from 1989 indicates that Iceland was not self-sufficient in Factor VIII products and no indication was given as to whether they intended to become self-sufficient at a later date.[103] No data was provided in relation to the relative use of cryoprecipitate and factor concentrates in 1986.[104] However, in 1989, Iceland used 1,300,000 IU of Factor VIII 'Ultra' and did not use cryoprecipitate.[105]

Spain

56. Media reports in 1985 indicated that at that time 50% of the plasma used in Spain was imported, mainly from the USA[106]. In 1986 Spain responded to a questionnaire of the Europe Committee of Experts on Blood Transfusion and Immunohaematology and reported that it imported 260,243 litres of plasma[107] and collected 859,000 litres of whole blood domestically.[108] Another document states that, in 1986, 100% of Spain's Factor VIII and Factor IX concentrate was

[99] RLIT0000462.
[100] NHBT0004514_017 at p.4; NHBT0004024_003 at p.3.
[101] SBTS0003019_002 at p.4.
[102] RLIT0000462.
[103] NHBT0010040_001 at p.28.
[104] PRSE0003860 at p.11.
[105] NHBT0010040_001 at p.27.
[106] DHSC0002275_061.
[107] NHBT0010040_001 at p.5.
[108] NHBT0010040_001 at p.14.

imported, with the source country / countries of those imports being unclear.[109]

57. In 1989 Spain reported importing 163,663 litres of plasma[110] whilst collecting 946,000 litres[111] of whole blood the same year. In one document it appears that the imported plasma was all sourced from outside of Europe, however subsequently the document records that 3,572 (no units given) Factor VIII concentrate *"in the form of plasma"* was imported from Austria.[112] Importation of Factor VIII is recorded with figures given of 1,000 kg cryoprecipitate from Korea, 200 kg cryoprecipitate from Germany and 890 kg cryoprecipitate from the USA as well as *"41.413 in the form of plasma from USA"*.[113] Another document records that 40 million IU of Factor VIII was imported in 1989 from the USA.[114] In information provided to the Council of Europe in 1989, Spain indicated that it did not know when it would become self-sufficient.[115]

58. A single treatment centre in Spain responded to a survey from the World Hemophilia AIDS Center in 1987 and, according to the publication Hemophilia World, indicated that the centre had 315 patients and had been using heat-treated or alcohol-precipitated U.S. and European derived concentrates since November 1983.[116] The 315 patients at that centre were approximately 1/5 of the total patients in Spain.[117]

59. In 1989 Spain reported using 15.4 million IU cryoprecipitate, 14 million IU of intermediate purity concentrate, 48.4 million IU high purity concentrate and no ultra pure concentrate.[118]

[109] PRSE0003860 at p.12.
[110] NHBT0010040_001 at p.4.
[111] NHBT0010040_001 at p.14.
[112] NHBT0010040_001 at pp.17 and 20. Although it is unknown whether the original source of the plasma was from Austria or imported into Austria.
[113] NHBT0010040_001 at pp.17 and 20.
[114] DHSC0002517_006 at p.3.
[115] NHBT0010040_001 at p.28.
[116] BART0000619 at p.5.
[117] NHBT0010040_001 at p.27.
[118] NHBT0010040_001 at p.27.

Italy

60. Until 1988, there was no official data of the population with bleeding disorders. Consequently, reports of numbers varied considerably and were said to be up to 10,000 Italians. Subsequently, it appears that figures were reported as approximately 4,000.[119] Data from 1986 suggests that there were 1,829 people with haemophilia A who were regularly treated and 1,614 in 1989.[120]

61. The blood system in Italy has been described by one academic as having developed in an *"uneven"* manner with a divide between the north and south of the country, in that *"the 'gift philosophy' toward blood has always been more accepted in the north than in the south, where notions of group loyalty did not foster the giving of blood by anonymous donors to anonymous recipients".* There was also a lack of national policy until the Collection, Preservation and Distribution of Human Blood Act in 1967, which regulated every detail of the process, but did not ban the sale of blood or blood products.[121] In 1971, a Presidential Decree was issued to regulate blood transfusion services and banned individuals with certain diseases from donating including those who had had or were currently suffering from viral hepatitis. [122]

62. In response to a Council of Europe questionnaire, Italy stated that in 1986 it had obtained 100,000 litres of plasma from whole blood and 2,000 litres from plasmapheresis donations within Italy. In 1989, this had increased to 210,000 litres from whole blood and 15,000 from plasmapheresis.[123]

63. However, in terms of blood products, in the early 1980s, Italy was importing 95% of its blood products, largely from the USA.[124] By 1986 it appears that all the Factor VIII and Factor IX concentrate that was being used in the country was being imported with no designation of the country of origin of the

[119] RLIT0000456 at p.236.
[120] NHBT0010040_001 at p.25.
[121] RLIT0000456, at p.231.
[122] RLIT0001966.
[123] NHBT0010040_001 at p.16.
[124] RLIT0000456 at p.229.
[125] PRSE0003860 at p.11.

plasma.[125] Data indicates that in 1986 Italy imported 47.5 million IU from the EEC and none from anywhere else. However, by 1989 they imported 3 million IU from EEC countries and 27 million IU from outside Europe.[126] In relation to plasma, in 1989, 30,000 litres of plasma were imported from EEC countries and 570,000 litres from outside Europe.[127] In Italy's Council of Europe questionnaire response in 1989, there is no data as to whether the product being used was cryoprecipitate or concentrate, and if it was concentrate whether it was of intermediate, high or ultra pure purity.[128]

Australia

64. From 1961, Commonwealth Serum Laboratories ("CSL") was the statutory authority responsible for the production and distribution of plasma sourced from human blood. The Australian Red Cross established and maintained a Blood Transfusion Service ("BTS") in each State and Territory. In addition, State Departments of Health operated localised blood banks from the 1980s.[129]

65. Donations were from voluntary, un-remunerated donors. However, the Senate Community Affairs References Committee report, *Hepatitis C and the blood supply in Australia*, recorded that collections from prison inmates continued until the mid-1970s in New South Wales, 1975 in South Australia, the early 1980s in Western Australia, and 1983 in Victoria and Tasmania.[130]

66. Factor VIII concentrate was made by CSL from the late 1970s.[131] It appears that by 1982, some divisions of the Red Cross were also manufacturing Factor VIII.[132] A Factor IX concentrate (Prothrombinex) was also developed by CSL and was "*the major form of treatment for haemophilia B until it was replaced with a purer Factor IX concentrate*

[125] PRSE0003860 at p.11.
[126] NHBT0010040_001 at p.21.
[127] NHBT0010040_001 at p.17.
[128] NHBT0010040_001 at p.27.
[129] MACK0002565 at p.17.
[130] MACK0002565 at p.55.
[131] MACK0002565 at p.56.
[132] PRSE0002045 at p.2.

(Monofix)".[133] It appears that no factor concentrates were imported into Australia.[134]

67. The plasma for the Factor VIII was predominantly supplied from the Red Cross.[135] However, the Senate report stated that prior to 1984, CSL blended Australian and New Zealand plasma for the manufacture of clotting agents. The evidence the Senate Committee received was that other than blending Australian and New Zealand plasma, CSL did not import or purchase any other plasma.[136]

68. According to Dr Peter Schiff, Research and Development Director of CSL from 1975 and Executive Director, Blood Products Division from 1987, in a statement prepared for civil proceedings in Australia, on average 5 donations were required to produce one litre of plasma for use in Factor VIII. In 1980, CSL used approximately 150 litres of plasma per production run, rising to approximately 300 litres per production run in 1985 and approximately 600 litres in 1989. In this statement, Dr Schiff stated that this meant that by 1989 CSL's production run of 600 litres could have used between 2,500 and 3,000 donations.[137]

69. In legal advice which appears to have been provided to the insurance company of the Australian Red Cross Society in civil proceedings concerning contaminated blood products,[138] it is stated that each batch of Factor VIII *"has an identifying number and was prepared from pools of donated plasma, containing plasma from up to approximately 2500 donations"*.[139]

70. In an article in the Lancet in 1982, it was reported that the Red Cross Blood Transfusion Service prepared Factor VIII concentrates from a pool of approximately 500 donations, and CSL prepared factor concentrates from a pool of 1,500 donations.[140]

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[133] MACK0002565 at p.56.
[134] PJON0000172_050 at p.13.
[135] CBLA000066_007 at p.1.
[136] MACK0002565 at p.54.
[137] CBLA0000066_007 at pp.1-2.
[138] PJON0000172_049.
[139] PJON0000172_050 at p.15.
[140] PRSE0002045 at p.2.

71. As to the usage of concentrates, the 1982 Lancet article, studying 243 people with haemophilia from 1977 to 1981, found: "*Commercial blood products are not used in Australia, and the patients were treated with products of blood from unpaid donors screened for hepatitis B surface antigen. Cryoprecipitate was the major treatment product, and only small amounts of factor VIII and IX concentrate were used...*"[141]

72. The study observed that Australia used much less Factor VIII for treatment of patients with severe haemophilia A than was used in major centres in the UK, USA and West Germany: "*If the Australian haemophiliac population is taken as 1200, approximately 22,000 units of factor VIII are available per severe patient per year. This figure is about 25%, 50% and 75% of the amounts used, respectively, in West Germany, the USA, and the UK.*" [142]

Knowledge of risk: Hepatitis

73. On 23 June 1967, the Belgian Association for the Study of Haemophilia held a Symposium on "*The Preparation and Use of Cryoprecipitated Factor VIII in Haemophilia*". Participants were from Belgium, France, Sweden, Norway, Netherlands, Finland and the UK. Prior to the symposium, participants were asked a series of questions about the *"rationale of the preparation of cryoprecipitated-Factor VIII and its clinical use in Haemophilia"* for discussion at the roundtable conference.[143] One of those questions was "*Is viral hepatitis more frequent after plasma transfusion (or fractions) compared to cryoprecipitate therapy or the reverse*?" Five doctors are recorded as providing answers. Dr Creveld (from the Netherlands) reported no incidents of hepatitis in their patients with haemophilia, as did Dr Pool (USA). Dr Prentice (Scotland) had a single patient who developed mild hepatitis over two days and recovered rapidly. Another Dutch doctor, Dr Loeliger, explained that he had treated one patient "*with very severe hepatitis after administration of cryoprecipitate...we have seen in Leiden many cases of hepatitis in patients who had plasma or plasma fractions administered. Two of the 13 patients receiving cryoprecipitate...developed subsequently*

[141] PRSE0002045.
[142] PRSE0002045 at p.3.
[143] HSOC0000617 at p.7.

hepatitis." Dr Verstraete (Belgium) was of the view that reports in the literature "*…are mentioning hepatitis after cryoprecipitate treatment. It is however extremely difficult to estimate if the incidence of hepatitis is greater after cryoprecipitate administration compared to whole plasma or plasma fraction I-0 treatment. The treatment with cryoprecipitate fraction VIII is too novel to have enough cases collected in order to make a fair comparison with other sources of human factor VIII*". [144]

74. In April 1970 a paper was submitted to the Sub-Committee of Specialists on Blood Problems of the Public Health Committee of the Council of Europe, titled *Hepatitis Associated Antigen and the Antibody to it*. The name of the author is obscured in the document.[145] The paper states that: "*In the last 12 months advances of greatest importance have been made in the knowledge of the antigen designated, in 1965, by Blumberg, Alter and Visnich, as Australia antigen…The term hepatitis associated antigen (HAA), proposed at a meeting in the USA in 1969 (McCollum 1969) is probably preferable, certainly until it is known with certainty whether the antigens so far described are in fact identical and until the relationship of the antigen (or antigens) with infectious hepatitis (hepatitis A or IH or short incubation hepatitis), serum hepatitis (hepatitis B or SH or long incubation hepatitis) and other forms of hepatitis has been worked out… The generally observed distinction between these forms of hepatitis may, of course be artificial. What is clear, however, is that the antigen is present during viral hepatitis as well in the blood of patients suffering from other certain diseases*."

75. In respect of the risk of transmission of what would become known as Hepatitis B, the paper observed; "*Certain individuals are apparently carriers of the antigen which may persist in their blood for long periods (see Zuckerman and Taylor (1969)). Transfusion of blood containing antigen was shown by Gocke et al (1969) to be followed by hepatitis (anicteric or icteric) in 9 out of 12 patients; 4 out of 75 surveyed, who were given antigen-negative blood, developed hepatitis. These authors found 16 antigen-positive donations among 2,211 donations tested … they do not say whether the donors of this blood were paid or unpaid*".

[144] HSOC0000617 at p.79.
[145] PRSE0000004.

76. The paper made observations in respect of the risk from transfusion: "*Although a close association between hepatitis and HAA has been demonstrated, a similarly close association between hepatitis and the antibody to HAA is less well established. Taylor et al (1969) and Almeida and Waterson (1969) described the finding of antigen-antibody complexes in patients with serum hepatitis. Hepatitis following transfusion may in fact occur while antibody is present in the blood (Holland et al 1969). Similarly, there are very few reports of the development of antibody following hepatitis. Antibody is usually found in the blood of multiply transfused persons. Experience in the UK suggests that antibody carriers among multiply transfused patients are considerably fewer than in the USA. This observation may be related to the fact that only blood from voluntary donors is used in the UK. See for example Walsh et al (1970), whose report provides further evidence that the hepatitis carrier rate among paid donors in the USA is considerably greater than among unpaid donors."* It was reported that the study by Walsh found hepatitis in 42 of 82 patients undergoing open heart operations who were given blood from paid donors, and no hepatitis in 28 patients undergoing similar operations, who received blood from unpaid donors.

77. The report recommended that because it was understood there was a very close association between hepatitis associated antigen ("HAA") and hepatitis, and the administration of blood and blood products containing the antigen might be followed by hepatitis in the recipient, donors should be routinely screened for the presence of the HAA antigen and debarred from giving blood if it was present. However, the recommendation came with the caveat that "*because of the obvious implications of routine screening"* consideration should be given to deferring its implementation until more was known about the HAA antigen, the corresponding antibody, and its relationship to hepatitis. The report stated that the introduction of screening in a piecemeal manner had "*obvious disadvantages*" and could not in any event be adopted until supplies of antisera were in place.

78. A report in the British Medical Bulletin from 1972, *Hepatitis in Transfusion Services*[146], compiled several recent studies from different countries or regions in respect of Australia antigen, as it was then referred to, in blood donors.

[146] CBLA0000123.

79. It is difficult to make direct comparisons between the countries because the number of patients involved in each study varied widely, the studies were conducted over a range of dates between 1968 and 1971, and little is known of the methodology in each study. With those limitations in mind, the compilation of studies from this report may provide a broad snapshot of prevalence amongst blood donors in the late 1960s to early 1970s. A summary of the studies in countries where a single whole-country study of unpaid donors[147] was obtained is as follows:

Country	Number tested	Method	Antigen present	Antibody present	Year of publication[148]
Australia	56,140	ID	63 (0.11%)	Not stated	1971
Belgium	6,656	ID	10 (0.15%)	26 (0.4%)	1970
Denmark	10,000	IEOP	18 (0.18%)	28 (0.28%)	1971
France	18,046	ID	75 (0.41%)	61 (0.34%)	1970
Germany	2,053	ID	17 (0.8%)	Not stated	1970
Japan	5,246	ID	54 (1.03%)	Not stated	1968
Japan (paid)	849	ID	19 (2.26%)	Not stated	1968
Kenya	200	ID	12 (6%)	Not stated	1971
Norway	3,162	ID	5 (0.16%)	1 (0.03%)	1970
Switzerland	2,641	ID	5 (0.2%)	Not stated	1970
ID = immunodiffusion, IEOP = immunoelectro-osmopheresis					

80. The report also reproduced the results of several studies into paid and unpaid donors in New York and Boston, USA. The results cannot be directly compared because they involve different test methods and different numbers of participants, but they offer some insight into the difference in prevalence rates in those cities:

City	Number tested	Method	Antigen Present	Antibody present	Study and year of publication
Unpaid donors					

[147] With the exception of Japan, where a second study into paid donors is marked as such.

[148] Year taken from reference for each study (see CBLA0000123 at p.2). It is not clear what the date range of the testing was.

New York	85,539	ID	84 (0.9%)	Not stated	Cherubin & Prince (1971)
Boston	106,294	ID, IEOP	114 (0.11%)	Not stated	Kilman et al. (1971)
New York	3,855	ID IEOP	17 (0.44%) 18 (0.47%)	Not stated	Gocke (1971)
Paid donors					
New York	1,961 2,007	ID ID	21 (1.07%) 24 (1.19%)	Not stated Not stated	Cherubin & Prince (1971)
Boston	1,170	ID	18 (1.5%)	Not stated	Kilman (1971)

81. In 1973 the Council of Europe produced a report called *Action by Council of Europe on Blood Problems: Activities of the Sub-Committee of Specialists on Blood Problems 1969-1973*, setting out the main achievements of the committee over the four years. [149] In its summary of work on blood transfusion and safety provisions, the Committee noted: "*Treatment with human blood and certain blood products is accompanied by a risk of transmitting hepatitis. This is usually due to the presence in the donor's blood of hepatitis B antigen (also called Australia antigen, Australia-hepatitis-associated antigen). This infective agent can be detected by certain laboratory tests and the sub-committee has recommended that all donations of blood should be tested for the presence of hepatitis B antigen.*"[150]

82. Two recommendations relevant to the risk of hepatitis B had been made by the sub-committee:

    i) "*<u>Recommended Measures on Australia Antigen (1971)</u>*

    The sub-committee strongly recommend that national authorities of member countries should give the control of hepatitis urgent consideration and high priority with a view to making it possible for all donors to be tested for the presence of Australia antigen."[151]

[149] SCGV0000075_052.
[150] SCGV0000075_052 at p.8.
[151] SCGV0000075_052 at p.16.

ii) *"Recommended Measures on the Organisation of Blood Transfusion (1973)*

The attention is drawn to the undesirable effects resulting from commercialisation of blood and derivatives and particularly as this applies to plasmapheresis programmes. Therefore it is recommended that all collection of blood including plasmapheresis should only be undertaken by government organisations or organisations working on a non-profit basis, with the authorisation of the government. The blood donations should preferably be on a non-remunerated basis.

2. It is recommended that all the activities in relation to blood transfusion, from the taking of the blood from donors until the administration of blood and its derivates to patients, should be the responsibility of physicians.

3. It is recommended that all such activities be subject in all member states to legislation or, if this is not feasible, to official regulations or recommendations. Such provisions should be based on the non-commercialisation of blood and on the medical responsibility, as defined in the recommendations (1) and (2) above."[152]

83. The Council of Europe Sub-Committee of Specialists on Blood Problems met in May 1974. A report of its meeting includes a note of a discussion of the issue of control of post-transfusion hepatitis. Reports from Dr W d'A Maycock (UK), Professor J P Soulier (France), and the Rosenheim Committee were considered. The sub-committee discussed the sensitivity of various methods of detecting hepatitis B and its antigen and it was noted that "*it appeared that in all countries the technique of immunoelectrosmopheresis (IEOP) was routinely used to screen donors but most countries were considering the introduction of more sensitive method such as reversed passive haemagglutination. In a few instances the radioimmunoassay (RIA) was used to screen donors; in others RIA was used to test pools of plasma which were to be used for preparing blood products*."[153] The sub-committee found that there were considerable differences between the sensitivity of RIA vs. IEOP and 25-50% as many confirmed positives were detected with RIA, depending which reports were relied on. It concluded that more experience

[152] SCGV0000075_052 at p.21.
[153] SCGV0000075_045 at p.27.

and investigation was necessary; RIA was an expensive and time-consuming method for use with all donations and was potentially of great value for examining pools of plasma.

84. On 29 May 1975, the World Health Assembly passed the following resolution:

"WHA28.72 Utilization and supply of human blood and blood products

The Twenty-eighth World Health Assembly,

Conscious of the increasing use of blood and blood products;

Having considered the information provided by the Director-General on the utilization and supply of human blood and blood products;

Bearing in mind resolution XVIII of the XXII International Conference of the Red Cross;

Noting the extensive and increasing activities of private firms in trying to establish commercial blood collection and plasmapheresis projects in developing countries;

Expressing serious concern that such activities may interfere with efforts to establish efficient national blood transfusion services based on voluntary nonremunerated donations;

Being aware of the higher risk of transmitting diseases when blood products have been obtained from paid rather than from voluntary donors, and of the harmful consequences to the health of donors of too frequent blood donations (one of the causes being remuneration),

1. THANKS the Director-General for the actions taken to study the problems related to commercial plasmapheresis in developing countries;

2. URGES Member States:

(a) to promote the development of national donation of blood services based on voluntary non remunerated donation of blood;

(b) to enact effective legislation governing the operation of blood services and to take other actions necessary to protect and promote the health of blood donors and of recipients of blood and blood products;

3. REQUESTS the Director-General :

(a) to increase assistance to Member States in the development of national blood services based on voluntary donations, when appropriate in collaboration with the League of Red Cross Societies;

(b) to assist in establishing cooperation between countries to secure adequate supply of blood products based on voluntary donations;

(c) to further study the practice of commercial plasmapheresis including the health hazards and ethical implications, particularly in developing countries;

(d) to take steps to develop good manufacturing practices specifically for blood and blood components in order to protect the health of both donors and recipients; and

(e) to report to the World Health Assembly on developments in these matters."[154]

85. In 1976 the International Society of Blood Transfusion issued Part 1 of a Guide, "*Criteria for the Selection of Blood Donors*".[155] This included a section on viral hepatitis which stated: "*In spite of recently developed tests for the detection of HBsAg, only a relatively small proportion of carriers can presently be detected. No routine screening test is presently available for the detection of hepatitis A virus, or of other viral agents that cause transfusion-associated hepatitis. It follows, therefore, that some general precautions should be taken in an attempt to reduce the risk of such viral agents being transmitted from donor to recipient.*

Prospective donors should be excluded if it is known that they:

1. Give a history of viral hepatitis at any time, except during the first months of life. (This rule may not be acceptable in all countries and may have to be modified where viral hepatitis is endemic.)

2. Have received a transfusion of blood or blood products within the last six months.

3. Have been in close, household contact with a case of" infectious hepatitis" in the last six months.

4. Have donated blood which was strongly suspected of having been responsible for a case of post-transfusion hepatitis.

5. Are suspected to be parenteral drug addicts.

6. Have been tattooed*, had their ears pierced, or experienced acupuncture within the past six months.*

7. Are inmates of a correctional institution.

8. Are HBsAg positive.

[154] NHBT0006435_003.
[155] DHSC0002179_067.

9. Are working in high-risk areas such as haemodialysis centres."[156]

86. The Guide also contained a section on Plasmapheresis Donors:

"Plasma donors for the production of IgG, anti-D, Factor VIII concentrate, antisera, control reagents, etc. must be selected with greater care than ordinary blood donors…The criteria for selection of ordinary blood donors should apply. It is recommended that the donor be investigated by a physician. A physician with special knowledge of the procedures should train the staff carefully and assume direct responsibility for the procedure…

Donors of antigenic material must give no history of jaundice and be HBsAg negative as determined by RIA or a test of similar sensitivity; they should, if possible, be regular blood donors whose donations have never caused hepatitis in the recipients… Other tests for those submitting to serial plasmapheresis include a test for syphilis and an RIA or RPHA test for HBsAg at each apheresis. The donor's complete history should be subject to medical audit at regular intervals to determine whether he may remain in the programme."[157]

87. Part 2 of the 1976 International Society of Blood Transfusion Guide was *Hazards of Blood Transfusion*. In respect of hepatitis, it stated:

"*Jaundice appearing between about 15 and 180 days after transfusion of blood or blood derivatives may be caused by viral hepatitis. Hepatitis A has an incubation period of between about 15 and 50 days: spread is usually by the faecal-oral route. Hepatitis B infection has a longer incubation period of from about 40 to 180 days or more: spread is normally by parenteral injection, but other, non-parenteral, means of transmission occur. It is known, for example, that HBsAg (an antigen on the surface of the virus) is present in saliva, sweat, breast milk, and vaginal secretions. "Non-A, non-B" infection is thought by some to be the commonest form of post-transfusion hepatitis. The incidence of post-transfusion hepatitis is not known with any certainty, and doubtless varies widely from one area to another, as it will be much influenced by the prevalence of hepatitis virus carriers among blood donors and the level of immunity to hepatitis infection among blood recipients. Tests for HBsAg (previously called the hepatitis-associated or Australia antigen) are now available. Although*

[156] DHSC0002179_067 at p.12.
[157] DHSC0002179_067 at p.14.

these will detect no more than about 50% of hepatitis B virus carriers, no blood or blood product should be transfused unless the donor is known to have been negative for HBsAg. It is recommended that each blood donation should be tested by such a method as counter-immunoelectrophoresis or, preferably, radioimmunoassay (RIA) or reverse passive haemagglutination (RPHA). If fresh blood has to be transfused before the results of such tests are known, a donor who has been tested previously for HBsAg, and found negative should be used."[158]

88. In a report of the WHO Expert Committee on Viral Hepatitis, dated 9 November 1976, it was noted that progress had been made towards *"the specific diagnosis of viral hepatitis, thanks to which a new type of hepatitis unrelated to hepatitis A or B virus has been recognized. This new type is now the most common form of post-transfusion hepatitis in some areas."*[159]

89. In April 1977, the Council of Europe's Sub-Committee of Specialists on Blood Problems produced an updated report on its activities between 1969 and 1977. The warning about the risk of transmission of hepatitis through blood products was repeated, along with the recommendation that all donations should be tested for the presence of hepatitis B antigen.[160]

90. On 30 April 1980 the Council of Europe Committee of Ministers adopted Recommendation No. R (80) 5, concerning blood products for the treatment of people with haemophilia. It recommended to governments of member states to:

"II. Pursue the implementation of the recommendations indicated in the appendix hereafter with a view to reaching, as far as possible, self-sufficiency of member states and their medical professions, both in respect of antihaemophilia products and blood plasma required for their preparation." [161]

91. The appendix noted that there was a need for *"optimal use of blood and of all its components"* for ethical, economic and medical reasons. Moreover, they recommended

[158] PRSE0000799 at p.12.
[159] RLIT0001229 at p.9.
[160] SCGV0000075_066 at p.9.
[161] DHSC0002490_033 at p.1.

that *"The geographical origin and the type of donor population (remunerated or non-remunerated) of the plasma used for coagulation factor concentrates should be indicated on every vial, in view of the fact that the risks of transmission of infectious diseases, in particular viral hepatitis, may vary from one area to another and according to the conditions of recruitment of the donors."*[162]

92. On 11 September 1981 the Council of Europe Committee of Ministers adopted Recommendation No. R (81)14, on preventing the transmission of infectious diseases in the international transfer of blood, its components and derivatives, including that:

"*…national regulations be established concerning the importation of blood, its components and derivatives with a view to limiting as fully as possible potential health hazards due to the transmission of infectious agents; such regulations should, in particular, provide for the furnishing and of data on the donation and the preparation of such substances, that is (in addition to the results of any specific tests which may be considered necessary by the importing state) the name of the country in which the blood was given, the date of the donation or preparation and data concerning the identity of the donor…*"[163]

93. A paper, *"Factor VIII concentrate – now free from hepatitis risk: progress in the treatment of haemophilia",* was presented at the 1982 International Society of Blood Transfusion conference in Budapest.[164] The paper set out the use of heat sterilisation such that "*…thanks to a new manufacturing process, a safe Factor VIII concentrate is available. Experimental and clinical trials have confirmed its freedom from hepatitis risk.*" The paper noted that "*several studies*[165] *have demonstrated at the incidence of icteric hepatitis among patients with haemophilia is of the order of 15%. Assuming that anicteric cases are of the same frequency, the total incidence of hepatitis must be of the same order as that seen after the transfusion of 6 units of blood. The true figures are probably much higher, but the only way of ascertaining them was to investigate*

[162] DHSC0002490_033 at pp.1-2.
[163] PRSE0002566.
[164] SBTS0000316_013. This paper was forwarded by Dr P Foster, PFC, Edinburgh to Dr J Cash, SNBTS on 12.04.83: PRSE0002343.
[165] It is not clear if the studies relied on involve only German patients or are a mixture of German and international studies.

haemophiliacs who were receiving replacement therapy with Factor VIII for the first time. In such patients, hepatitis rates of 60% have been found. Radioimmunological techniques for detecting the markers of hepatitis B virus have shown that all patients receiving replacement therapy have in fact been exposed to the virus."[166]

94. The paper stated that from the increasing number of case reports "*it is apparent that here, too, there has been a shift in the virus spectrum similar to…post transfusion hepatitis, Type B having been partly replaced by Type non-A/non-B. The latter form has proved especially dangerous amongst patients with haemophilia, as it may occur despite the existence of immunity to hepatitis B and frequently runs a chronic course. Repeated attacks in the same patient have been reported. At present there are no specific markers for detecting non-A/non-B hepatitis…The risk of hepatitis among haemophiliacs had become very serious and urgent measures were required to combat it…* "[167]

95. The Council of Europe Select Committee of Experts on Automation and Quality Control in Blood Transfusion Services met on 8 to 11 March 1982.[168] A report was prepared by Erik Freiesleben (Denmark), *"The Criteria for Selection of Blood Donors"*. It included the following:

"*Donors with a history of viral hepatitis should be excluded. An accepted test for HBsAg shall be performed each time a donor is bled. … Individuals with a history of hepatitis are excluded from the donor panel. The same is true for persons, whose blood give a positive reaction for the presence of HBsAg. Otherwise, presence of anti-HBsAg does not debar. Persons who have been in house contact with hepatitis or received a transfusion of blood or blood products should have a quarantine period of 6 months…Donors having donated blood to two patients strongly suspected of having post-transfusion hepatitis should be excluded. This is also the case if a donor is the only donor of blood to a recipient with post-transfusion hepatitis.*"[169]

[166] SBTS0000316_013 at p.1.
[167] SBTS0000316_013 at p.3.
[168] NHBT0017489_001. It is unclear if the contents of the report are recommendations by the author, or a representation of what has been agreed by the committee.
[169] NHBT0017489_001 at pp.4 and 6.

96. At a meeting of the Committee of Experts on Blood Transfusion and Immunohaematology, Council of Europe on 21 May 1982, it was recorded that *"Committee members reported that it was generally recognised that the frequency of transfusion associated hepatitis was higher when using commercial plasma."*[170]

97. Quality Control Guidelines, drafted by the Council of Europe Select Committee of Experts on Automation and Quality Control in Blood Transfusion Services, were submitted to the Council of Europe's Committee of Experts on Blood Transfusion and Immunohaematology for approval at their meeting on 28 to 31 May 1984.[171] In respect of jaundice and hepatitis, it recommended: *"Individuals with a history of jaundice or hepatitis may, at the discretion of the appropriate competent authority, be accepted as blood donors provided an approved test for HBsAg is negative. Persons whose blood gives a positive reaction for the presence of HBsAg are excluded. Presence of anti-HBs does not debar. Persons who have been in close contact with a case of hepatitis or who have received a transfusion of blood or blood products should have a quarantine period of six months…Donors without demonstrable markers of hepatitis who have donated blood to two patients strongly suspected of having transfusion-transmitted hepatitis should be excluded. The only donor of blood to a recipient with transfusion transmitted hepatitis should also be excluded."*[172]

Sample countries: Knowledge of, and response to, Hepatitis prior to the advent of AIDS

Netherlands

98. Testing for hepatitis B antigen was started in about 1972 and was mandatory from 1973, under the Law of Human Blood.[173]

[170] PRSE0000809.
[171] SBTS0000151_007.
[172] SBTS0000151_007 at p.12.
[173] CBLA0000058_036 at p.27.

99. In a study published on 10 January 1981 in the British Medical Journal, blood samples were taken in 380 post-transfusion patients in the Netherlands. The results "*indicated that 15 of the 380 recipients developed hepatitis; all were asymptomatic. In the absence of a practicable test for non-A, non-B antigen or antibody 13 of these patients, in whom cytomegalovirus, hepatitis A, and Epstein-Barr viruses were not implicated, were considered to have post-transfusion non-A, non-B hepatitis*…." The authors commented that: "*There is a controversy in published reports about the value of increased ALT activities in donor blood in predicting the development of post-transfusion, non-A, non-B hepatitis. Some investigators found that the likelihood of developing such hepatitis increased greatly when the ALT activity in donor blood exceeded 45 IU, while others could not confirm these findings. In our group of 38 donors whose blood was implicated in post transfusion non-A non-B hepatitis the highest activity of ALT was 21 IU. This fact, together with the fact that only volunteer blood is used in the Netherlands, may explain the lower incidence of post-transfusion non-A non-B hepatitis in our group (3.4%) than in the US (5.4-18.5%). Furthermore, because of our liberal criteria for diagnosing non-A non-B hepatitis, its real incidence in our patients may have been even lower. Nevertheless, the finding that 3.4% of a group of recipients of donor blood that had been screened for HBsAg developed non-A, non-B antigen(s) emphasises the need for practicable methods of detecting non-A, non-B antigen(s). Furthermore, such methods are needed for studying the causal role of non-A, non-B agent in "autoimmune" chronic active hepatitis and in the serological diagnosis of acute hepatitis"*[174]

Germany

100. The Council of Europe Committee of Experts in Blood Transfusion meeting report dated August 1987 recorded that ALT testing had been used in the Federal Republic of Germany and some regions of Italy since 1965.[175] At that meeting, Professor H. Weise remarked that ALT testing had been used in the Federal Republic of Germany for more

[174] NHBT0000114_027.
[175] NHBT0008816_002 at p.5.

than 20 years, and the reduction of NANB hepatitis was estimated to be 29%, although no controlled studies had been carried out." [176] Another document notes that ALT was *"recommended in 1965 by the German Society for Hospital Hygiene. It is a legal requirement but there is no uniformity in exclusion levels."*[177]

101. In 1978 a clinical trial of heat treated product started[178] and on 13 August 1981 a federal letter was sent to clinic directors that all HBV negative patients should be treated exclusively with hepatitis safe (reduced) products and the higher cost should be borne.[179] This was not universally implemented.

102. By the time that the first heat-treated Factor VIII product was licensed in Germany in February 1981, Stephen Dressler, a German physician, states that the majority of people with haemophilia in West Germany were already infected with hepatitis B. Moreover, he states that 66% of patients already suffered from chronic liver disease. From 1978 to 1987, hepatitis B linked cirrhosis caused 18% of deaths amongst people with haemophilia in West Germany.[180]

103. In 1983, a study published by Schimpf found that *"As a result of the frequent application of factor VIII and IX concentrates of single donor cryoprecipitates as well as of concentrates from large plasma pools a very important side-effect became evident: the transmission of serum hepatitis in its two forms B and Non A Non B. Dependent on the factor dosage, up to 100% of patients showed signs of an active hepatitis or contact of the defense system with hepatitis viruses. With increasing frequency of chronic hepatitis (65%) there is also an increase in the aggravation of liver cirrhosis which manifests itself 13 years earlier than in the normal population".*[181]

Belgium

[176] NHBT0008816_002.
[177] NHBT0000018_019 at p.19.
[178] RLIT0001934 at p.45. See also PRSE0004058.
[179] RLIT0001934 at p.67.
[180] RLIT0000456 at p.212.
[181] PRSE0002234.

104. In a report dated 1981, Dr Gunson noted that in Belgium, donors were subject to a number of blood tests including ALT and hepatitis B at their first donation. Hepatitis B testing was repeated at each donation. A full medical examination including ECG was performed at the second or third visit.[182]

Denmark

105. In an article in May 1974, M. Bjorneboe described studies using liver biopsies, from 1941 onwards, to show a transition from hepatitis to cirrhosis, alongside epidemiological studies in Scandinavia dating from 1930. After detailing studies of the connection between hepatitis B antigenaemia and cirrhosis, he concluded that *"It must now be accepted as a fact that hepatitis can lead to cirrhosis. The relative importance of this aetiology is more difficult to decide as long as specific sero reactions are not available."*[183] He also noted that *"the frequency of cirrhosis caused by hepatitis is different in the different age groups and in the two sexes. The frequency is higher for women than for men, and increases with increasing age"*.

106. It appears that "*screening of donor blood for Hepatitis B was fully implemented in Denmark by 1 June 1983, and from then on also functioned as a surrogate marker for AIDS*."[184] It is unclear to what extent testing was undertaken in Denmark before this point, and at what point partial testing for hepatitis B was first introduced.

Finland

107. A *Scandinavian Journal of Haematology* article reported that the Finnish Red Cross Blood Transfusion Service started donor hepatitis B antigen screening in spring 1970 on a limited scale at four centres and that it was extended gradually. By the end of 1970 all

[182] CBLA0000042_113 at p.5.
[183] RLIT0001922 at p.4.
[184] RLIT0000456 at p.180.

donors in Finland were being tested for HBsAg at least once, with some tested twice. From September 1973, all donors had to be tested at every donation.[185]

108. In 1982 a study was undertaken of 65 post-transfusion heart surgery patients for NANB hepatitis. Three cases of post transfusion NANB hepatitis were found, representing 4.6% of patients and a rate of infected blood units at 0.5%.[186]

109. Between 1985 and 1988 the prevalence of HBsAg positivity in new Finnish blood donors was 0.05%. The incidence of reported transfusion hepatitis was 10 cases per year in the early 1970s and 0-6 per year during the 1980s, from approximately 300,000 annual transfusions.[187]

110. As at September 1988, a prospective study was being carried out at all five university hospitals with about 300 patients enrolled in it, and donors were being tested for ALT, anti-HBc, guanase and GT.[188]

Italy

111. As noted above, a decree of the President dated 24 August 1971 mandated that where donors were found, on general medical examination, to have or have had viral hepatitis then they would not be accepted as donors (Article 46).[189] Moreover, a person was temporarily prevented from donating blood if they had *"received in the last six months a transfusion of blood, plasma, fibrinogen or other derivatives that can transmit hepatitis"* (Article 47).[190]

112. It appears that screening blood for hepatitis B surface antigen and serum alanine aminotransferase was introduced in the early 1970s.[191] Screening for

[185] PRSE0002287 at p.10.
[186] PRSE0002720 at p.3.
[187] NHBT0000101_039 at p.15-19.
[188] NHBT0000018_019 at p.20.
[189] RLIT0001965.
[190] RLIT0001966.
[191] NHBT0085294_004 at p.3.

surrogate markers, such as antibody to hepatitis B core antigen, was never undertaken.[192]

113. Although testing was required, it does not appear that a particular generation of test was required until 1977. The regulatory framework and the governmental speed in responding to issues in the blood supply have been criticised, by an Italian legal academic Umberto Izzo. One example that is used is the infection of people with hepatitis B through the use of Trilergan, an anti-allergenic drug containing immunoglobulins imported from the US in 1974. It took three years after this event before the Health Ministry drew its conclusions and required transfusion centres and the pharmaceutical industry to test each blood donation for hepatitis B surface antigen using a third generation method.[193]

114. As to the understanding of the risk of hepatitis in people with haemophilia, Professor Manucci reported in 2003, referring back to his study of liver function tests, published in 1975, surveying 91 multi-transfused Italian people with haemophilia, that: *"although non-A, non-B hepatitis virus(es) was suspected to be responsible for transaminase abnormalities, a definite distinction between transfusion-associated hepatitis and 'transaminase' … could not be made that time".*[194] In the 1975 paper, he had concluded that *"These data suggest that in haemophiliacs repeated and prolonged contact with the agent(s) responsible for post-transfusion hepatitis may cause chronic liver damage not associated with overt illness."*[195] Reflecting on the position in the 1970s, in his 2003 paper Manucci stated that *"unequivocal evidence of the existence of structural liver disease"* did not come until 1977, following the Lesesne paper[196], and that a *"relatively benign"* picture of non-A non-B hepatitis emerged from the Lesesne paper and a Colombo/Rizzetto study until this was questioned by studies in 1985 and 1986.[197]

[192] RLIT0001963.
[193] RLIT0000456 at p.233.
[194] HCDO0000243_035.
[195] PRSE0000240.
[196] PRSE0004172.
[197] HCDO0000243_035 at p.3.

115. Manucci also noted that the risk of chronic hepatitis was unacceptable for people with mild haemophilia. He undertook a trial of DDAVP demonstrating its effectiveness in April 1977.[198] He stated that the advantages in decreasing the risk of blood-borne infections were *"widely recognised"* in Italy.[199]

Australia

116. It is understood that Australia was the first country to introduce comprehensive hepatitis B screening: "*After the discovery of the specific antigen for hepatitis B, testing of blood started in late 1969, and by September 1970 Australia's blood supply was the first to be fully screened.*" The staff at Fairfield Infectious Diseases Hospital in Melbourne tracked the early spread of hepatitis B among drug users from Sydney, and a clinician based there, Dr Ian Gust, "*built an international reputation with his research on hepatitis A and B.*"[200]

117. A study from Australia, published in the Lancet on 23 January 1982, reported that in a study of 842 cardiac surgery patients, 2% of transfusion recipients developed transfusion hepatitis. 3 of the 18 cases were caused by hepatitis B virus even though all units of blood which contained hepatitis B antigen had been rejected. 1 case was caused by cytomegalovirus and there were 14 (78%) cases of NANB hepatitis.[201]

118. An article in the Lancet, dated 17 July 1982, reported on a study of 243 people with haemophilia in Australia from 1977 to 1981. The study found: "*Commercial blood products are not used in Australia, and the patients were treated with products of blood from unpaid donors screened for hepatitis B surface antigen. Cryoprecipitate was the major treatment product, and only small amounts of factor VIII and IX concentrate were used. Despite the use of blood products obtained from entirely voluntary blood donors and the frequent use of single-donor packs of cryoprecipitate, markers of viral hepatitis were common in these haemophiliacs. Antibody to hepatitis B surface antigen*

[198] HCDO0000243_035 at p.3.
[199] HCDO0000243_035 at p.3. See also BPLL0001352.
[200] RLIT0000456 at p.262.
[201] NHBT0000080_004.

was detected in 63% of the patients, and there were 66 cases of non-A, non-B hepatitis during the study; 29 of these episodes persisted for longer than 6 months. 13 patients (5.4%) had hepatitis B during the study; 2 patients remained HBsAg-positive for longer than 6 months. Abnormal serum aminotransferase levels were found in 34% of the patients; in 8% of patients these abnormalities persisted for more than 6 months."[202] The article concluded that the study emphasised the greater risk of liver disease and chronic NANB hepatitis for patients in receipt of mainly cryoprecipitate and some Factor VIII concentrate with severe haemophilia, compared with those with milder haemophilia. The study noted that the relatively high frequency of liver abnormalities in patients was disturbing, given that all the plasma for Factor VIII fractionation was supplied by voluntary, unpaid, hepatitis B screened donors.[203]

Knowledge of risk: HIV/AIDS

119. The Inquiry's chronology on Knowledge of risk[204] sets out many of the key events around the world (and particularly in the United States of America) that added to the knowledge of risk of HIV and AIDS and so should be consulted for a more in depth consideration of knowledge of risk. It is likely that knowledge in America spread to Europe.

International Forums

120. The first report of AIDS in the Western world appeared in the Mortality and Morbidity Weekly Report of the CDC (MMWR) on 5 June 1981, which listed five cases of PCP in homosexual males in San Francisco.[205]

121. The first cases of AIDS in patients with haemophilia were reported in the 16 July 1982 issue of MMWR.[206]

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[202] PRSE0002045 at p.1.
[203] PRSE0002045 at p.2. Letter to the Lancet (27 November 1982) (Gabra, Crawford, Mitchell) concurs: PRSE0001036.
[204] INQY0000006 and the transcript of the oral presentation of the chronology is at INQY1000056.
[205] CGRA0000242.
[206] PRSE0000523.

122. The Council of Europe, Committee of Experts on Blood Transfusion and Immunohaematology, met on 16 to 19 May 1983 to discuss AIDS. Countries were asked to provide information about the numbers of reported cases and the measures being taken regarding donor selection in response to AIDs.[207] A summary of the picture on the response to risk as at April/May 1983 is as follows:[208]

a. No measures had yet been taken in Ireland, Italy, Sweden, the United Kingdom or Finland.

b. In the Netherlands, clinicians treating people with haemophilia, had requested that no Factor VIII concentrates from the US should be used in the future.

c. The countries still formulating the approach to take were Denmark, Austria, Norway and Spain.

d. Belgium envisaged taking measures for donor selection (but had not implemented them).

e. The only countries said to have taken any measures were Germany (FDR),[209] Canada and Luxembourg. Canada had contacted and informed groups at high risk of developing AIDS both directly and through the media that they should self-exclude as blood donors. Luxembourg had temporarily excluded donors who had travelled to Haiti and had totally eliminated remunerated donors '*or if this is impossible, marking of remunerated and non-remunerated donors*' (it is unclear what this means).

123. Dr Gunson prepared a report of the meeting of 16 to 19 May 1983.[210] In respect of the severity of the risk, he recorded that it was recognised that "*the disease carries a high mortality rate*." The significance of AIDS to the Committee was recognised to be in relation to the transfusion of blood and blood products, particularly with coagulation factor concentrates given to patients with haemophilia. The report goes on:

"Absolute proof that AIDS is caused by a transmissible infectious agent is not yet available, but the consensus in the Committee was that it should be regarded as such and that a recommendation should be made to the Council of Ministers at the meeting

[207] DHSC0000717.

[208] Please note that the information provided by those countries which have their own section in this presentation note can be found in the individual country sections.

[209] The steps taken by Germany are set out in the section on Germany below.

[210] NHBT0017430.

in June to take necessary steps to minimise the transmission of AIDS by the transfusion of blood products."

124. In the absence of a specific test, the recommendations made at that meeting[211] included:
    1) To avoid the use of coagulation factors prepared from large plasma pools unless medically required, especially in countries where self-sufficiency had not been achieved.
    2) To inform physicians and selected recipients such as people with haemophilia of the potential health hazards of haemotherapy and the possibility of reducing those risks.
    3) To provide all blood donors with information on AIDS so that those in high risk groups would not donate.
    4) To pursue rapid and full implementation of Recommendations R (80) 5 and R (81) 4 – those being the recommendations about the need to achieve national self-sufficiency from voluntary, non-remunerated, donors.

125. The report suggested that it was understood at a European level that there was a heightened risk of HIV infection associated with large plasma pools, imported blood and blood products from high-risk donors, which could be mitigated by national self-sufficiency and information being given to donors to help high risk donors to refrain from donating.

126. On 23 June 1983 the Committee of Ministers adopted the recommendations of the Expert Committee on Blood Transfusion and Immunohaematology regarding the prevention of the possible transmission of AIDS from affected blood donors to patients receiving blood or blood products. Recommendation No. R (83) 8 was as follows:

"I.

a. To avoid wherever possible the usage of coagulation factor products prepared from large plasma pools; this is especially important for those countries where self-sufficiency in the production of such products has not yet been achieved;

[211] NHBT0017430.

b. *To inform attending physicians and selected recipients, such as haemophiliacs, of the potential hazards of haemotherapy and the possibilities of minimising these risks;*

c. *To provide all blood donors with the information on Acquired Immune Deficiency Syndrome so that those in risk groups will refrain from donating…*

II. to pursue rapid and full implementation of Recommendations No. R (80) 5 and No R (81) 14."[212]

127. In a press release dated 5 July 1983, the Council of Europe summarised the view of the Council of Europe's experts, and the experts in Canada and the USA, stating that although there was no formal proof of the transmissibility of AIDS through transfusion, there was a need to introduce measures in Europe in blood transfusion centres to prevent the contamination of patients receiving blood.[213] The press release concluded that voluntary donations remained the best safeguard for non-contamination of blood products and that "*the health of all Europeans is at stake.*"

128. A Forum Council of Europe publication dated 1983 by a Dr Kalogjera on measures to combat AIDS, stated it was recognised that AIDS can be transmitted sexually and by transfusion. It was reported that the transmission of AIDS via transfusion had been reported amongst people with haemophilia receiving factor concentrates, particularly commercially produced Factor VIII concentrates prepared from large plasma pools from America.[214]

129. The World Haemophilia AIDS Centre (WHAC) was set up in late 1983 in response to the need identified by the World Federation of Haemophilia (WFH) for an international communication mechanism. Its goals were (i) to communicate with professionals who treat patients and with the public; (ii) to establish international epidemiologic surveillance of AIDS and haemophilia; (iii) to provide factual, timely information about haemophilia and AIDS; and (iv) to establish WFH-WHAC liaison with the US CDC, the WHO, and the League of Red Cross and Red Crescent Societies as well as blood and

[212] MACK0000307.
[213] BPLL0004935_102.
[214] BPLL0004935_086 at p.1, columns 1 and 2.

plasma collection agencies. In an article, written by Donna Bone about this (published in the Plasma Quarterly in winter 1984), she said '*no other agency had the international responsibility for gathering and disseminating data about cases of AIDS and AIDS-related complex (ARC) in persons with haemophilia'*.[215]

130. Between 19 and 21 October 1983, a meeting co-sponsored by the Danish Cancer Society, the World Health Organisation, and the European Organisation for Cooperation in Cancer Prevention Studies took place in Aarhus in Denmark. The specific aim of the meeting was set out in press release dated 30 September 1983:

1 *to compile, for immediate publication, the available information concerning AIDS in Europe so as to give a picture of the initial years of the occurrence of the epidemic in this part of the world;*

2 *to summarize, for immediate publication, the available information concerning two pressing clinical problems, namely the early prodromal symptoms of AIDS and the effectiveness of the different therapeutic strategies;*

3 *to draw up a set of recommendations concerning preventative measures for the use of European health authorities and WHO;*

4 *to establish a permanent international monitoring system in Europe and to develop research projects on the disease that should be carried out on a collaborative basis by countries in Europe and other parts of the world.* [216]

131. A summary of the conference (prepared by someone at the DHSC Med IMCD division) noted that as of 19 October 1983, there had been 2,508 reported cases of AIDS in the USA and 267 in Europe. [217] The recorded incidence rate of AIDS in people with haemophilia was *'1 per 1,000 haemophiliacs both in the USA and Europe'*. It was suggested that *'all the countries in Europe should aim*

[215] BAYP0005567 at p.3.
[216] PRSE0000911.
[217] PRSE0000031.

to become self-sufficient in blood products at the earliest possible date' and a European *'AIDS Task Force'* should be established.

132. A full report of the meeting was due to be published in the European Journal of Cancer and Clinical Oncology.[218] It set out the recommendations emerging from the conference which included:

> *"Information and advice to physicians*
> *It is recommended that special efforts be made to inform the medical profession about the emergence of the infectious disease AIDS. This comprehensive information shall include a description of AIDS, a list of useful diagnostic procedures, a list of hospitals experienced in treating AIDS and of laboratories which perform the necessary special immunological or serological tests.*
> *Due to the nature of the disease and the prevalence of AIDS in certain groups AIDS patients will be seen by general practitioners or specialists in haematology, dermatology, venereal diseases, proctology, urology, infectiology or who care for haemophiliacs. Those physicians should be informed about AIDS via their professional organizations and be provided with registration forms.*
>
> *Advice to the public*
> *It is not surprising that AIDS has attracted great public interest. The rights of the public to be informed must be respected. Therefore all pertinent information should be made available using established channels of communication. At the same time all appropriate authorities, all physicians and researchers are urged to made sure that their statements to the press can not be misinterpreted or abused.*
> *On the basis of the presently available information advice to the public in Europe could read as follows:*
> ……
> *Cases of AIDS have been observed among recipients of coagulation factors prepared from blood of several thousand of different donors. Such preparation are*

[218] ARMO0000233.

administered to patients with rare bleeding disorders. As a consequence the rules for the selection of blood donors have been altered in order to prevent the collection of blood that my contain the AIDS-agent.

Although AIDS has been recognised only recently, enough information has been gathered to state today that AIDS poses no risk to the public at large. Casual or social contacts with AIDS patients, e.g. in subways, in restaurants, on lavatories or in private homes carry no risk to acquire AIDS.

Advice to recipients of blood coagulation factors and their physicians

The acquired immune deficiency syndrome (AIDS) has been observed in haemophiliacs receiving factor VIII or factor IX concentrates. Since in 1982 the infectious nature of AIDS became apparent special efforts have been made to select carefully the donors for plasma used to prepare coagulation factors. Research activities with the aim to manufacture coagulation factors synthetically or to process plasma in such a way that infectious agents are completely eliminated or destroyed are under way. It has to be expected that the risk of acquiring AIDS for haemophiliacs will decrease continuously in the near future.

It should be noted that the use of cryoprecipitate appears to carry a smaller risk than the use of large pool preparations. It has been suggested that newly recognised haemophiliacs who need substitution be treated only with cryoprecipitate. It is recommended to achieve national self sufficiency with regard to plasma used for production of coagulation factors from donors not at risk of hepatitis and/or AIDS.

The recommendations of the Council of Europe on Preventing the Possible Transmission of AIDS from Affected Donors to Patients Receiving Blood or Blood Products should be implemented."

133. In a letter dated 14 December 1983, Dr Walter Dowdle, Director of the Centre for Infectious Diseases (Centers for Disease Control, Atlanta), wrote to Dr J.G.Watt at the Protein Fractionation Centre in Edinburgh.[219] Dr Dowdle referred to a recent WHO meeting on AIDS and enclosed a draft of a paper titled: *Acquired Immunodeficiency Syndrome, An Assessment of the Present Situation in the World*. The draft was dated 12 December 1983 and was intended to be finalised by WHO. The Inquiry has been unable to locate the final version of the document.

[219] CBLA0001775.

134. The paper summarised position as follows: "*The acquired immunodeficiency syndrome (AIDS), a clinical entity that includes fatal opportunistic infections and otherwise rare malignancies, was first reported in the United States in 1981. In retrospect, the first cases had occurred in that country as early as 1978. Soon after these first reports in 1981 similar cases began to be reported from other areas of the world.*"

135. The section of the report on the epidemiology and surveillance in Europe stated: "*AIDS has been increasingly reported in many countries in Europe. (Table 3). Among citizens of European countries, the risk factors and demographic characteristics resemble cases reported in the United States, with over 70 percent of cases occurring in homosexual men. Fewer than 2 percent of cases have occurred in heterosexual abusers of intravenous drugs and 4 percent in persons with haemophilia. It is noteworthy that 59 (22%) of 268 cases reported in Europe have been reported among persons born in Africa.*"[220]

136. The report addressed the issue of how HIV was transmitted. It appears that by this stage there was international recognition that HIV was very probably transmitted by blood and blood products, including filter-sterilized blood coagulation factors:

"*The etiology of AIDS is unknown, but the epidemiologic pattern of AIDS is most consistent with its being caused by a transmissible agent. Transmission of the presumed agent of AIDS appears to occur by sexual contact, by blood sharing (either by therapeutic blood or blood products or by shared needles used for illicit drugs), or during the birth process (possibly intrauterine)…*

Although there are other etiologic possibilities, either alone or as cofactors, the most likely cause of AIDS is a virus. Support for this is based on observations that i) the disease distribution is similar to hepatitis B in many industrialized countries…3) AIDS occurs in recipients of filter-sterilized blood coagulation factors, therefore the putative agent should be capable of passing through such filters…"[221]

"*AIDS cases have infrequently occurred both in haemophiliacs receiving clotting factor concentrates and in recipients of blood and blood component transfusions who*

[220] CBLA0001775 at p.4.
[221] CBLA0001775 at p.13.

do not have other apparent risk factors. Approaches to reducing the possibility of spreading AIDS by blood and blood products include 1) educating the general public and donor groups, 2) excluding donors who belong to established risk groups, 3) avoiding non-essential use of blood and blood products, 4) and preparing and using blood and blood products in such a way as to reduce the risk of transmitting AIDS. The present recommendations are made in the absence of a specific, reliable laboratory test for AIDS. Should such a test become available, these recommendations will need to be reviewed...Some countries have recommended that persons with AIDS and members of populations with an increased incidence of AIDS voluntarily refrain from donating blood or plasma...A totally voluntary blood donor system was recommended in 1975 by WHO…"

"*Immunoglobulin and albumin prepared by generally accepted methods have not been implicated in AIDS and are considered safe. Coagulation factor concentrates, however, have been implicated in cases of AIDS. Although additional inactivation methods have recently been developed, it will not be possible to fully establish their effectiveness until the agent of AIDS is discovered. There are two approaches to minimizing the risk associated with processed plasma fractions: 1) reduce the number of donors contributing to the products a patient receives and 2) employ process technology aimed at reducing contamination risks. Plasma fractions may be produced from single donor material or from pools obtained from up to 20,000 donors. Since small-pool products expose patients to smaller numbers of donors than large-pool concentrates, individual patients regularly treated with small-pool products have a lower theoretical risk of exposure.*

Another approach to reducing the risk of AIDS from plasma fractions is to use specified donor material for a given recipient. An extension of that concept is to use a specified batch of material from a pool of a given size, thus reducing the number of donor exposures by the patient. Use of the specified donor-recipient approach for persons with newly diagnosed haemophilia requiring only infrequent therapy should be explored."[222]

137. A World Federation of Haemophilia (WFH) report from the Medical Board (an advisory board to the WFH) dated 29 June 1983 stated that:

[222] CBLA0001775 at p.20.

a. Following the recognition of AIDS in people with haemophilia, steps were being taken to exclude high risk donors from the US blood and plasma supply.
b. The commercial producers of concentrate acted swiftly to eliminate members of high risk groups by closing plasmapheresis centres in high risk areas and providing for self-exclusion by educational materials supplemented by medical screening and physical examination.
c. The precise cause of AIDS remained unclear.
d. There was insufficient evidence available to recommend any change in treatment for people with haemophilia, who were advised to continue with whatever blood product was available according to the judgement of their doctor.[223]

138. In July 1983 in the Newsletter of the League of Red Cross Societies entitled 'Transfusion International', the editorial (by Prof Leikola) observed:[224]

"There is relatively strong evidence indicating that the disease [AIDS] may be transmitted by blood. In the United States, it is reported that eleven haemophiliacs have contracted AIDS, and additional haemophiliacs with AIDS have been observed in Europe. There is a suspicion that commercial Factor VIII concentrate, prepared from large pools of US plasma, has been the source of infection.
Although there is no absolute proof that blood really does transmit AIDS infection, there is one case where the causal relationship is highly suggestive."

The editorial then went on to set out the facts of the San Francisco baby case reported in December 1982.[225]

139. On 12 January 1984 the New England Journal of Medicine published a study by Curran et al entitled '*Acquired Immunodeficiency Syndrome (AIDS) Associated with Transfusions*'.[226] This reported 18 suspected cases of transfusion-associated AIDS. The investigators of the study concluded that blood components could transmit AIDS, that exposure to only one infected unit might result in transmission, and that donors who had developed no symptoms of AIDS could be infectious.

[223] PRSE0001351.
[224] PRSE0002301.
[225] PRSE0003276.
[226] PRSE0001931.

140. According to the Krever inquiry report:[227]

"Dr. Zuck, an eminent U.S. blood banker and the director of the division of blood and blood products of the U.S. Food and Drug Administration between 1985 and 1987, said that the effect of the study was 'to put the whole medical community and perhaps the world on notice that AIDS is transmitted by blood transfusions, period.'"

141. On 5-9 March 1984 the Select Committee of Experts on Automation and Quality Control in Blood Transfusion Services met and drafted quality control guidelines.[228] The guidelines included a requirement to:

a. Evaluate the blood donor's health via their medical history – albeit recognising that "*a complete medical and physical examination of blood donors is generally not possible in practice. One has to rely upon the donor's answers to some simple questions regarding his/her medical history and general health combined with a simple inspection of donor's appearance and a few laboratory examinations.*"

b. Provide all blood donors with information on AIDS so that those in high-risk groups could refrain from donating.

142. The guidelines were put before the Committee of Experts on Blood Transfusion and Immunohaematology for approval at their meeting on 11 – 14 June 1985.[229] They were approved.[230] An amendment was made to the donor selection questionnaire by the Committee of Experts on Blood Transfusion and Immunohaematology at their meeting on 3 – 6 May 1988,[231] when they determined that two questions should be added to it, asking the donor first whether (s)he had read and understood the information on AIDS that had been given, and secondly whether (s)he belonged to any of the risk groups identified.

143. On 30 June 1984 Professor Bloom published a paper in the Lancet announcing the results of a survey of 135 European haemophilia centres in 18 countries.[232] Eight cases

[227] KREV0000001 at p.274.
[228] SBTS0000151_007 at p.11.
[229] NHBT0008468.
[230] NHBT0009084.
[231] NHBT0000018_019.
[232] PRSE0003037.

of AIDS had been identified, which when combined with other reports, was said to amount to an incidence of 11 cases in 13,000 treated patients with haemophilia. The average age of the infected person with haemophilia was 20 years and at least three patients were 14 years old or younger. One patient, from Portugal, had been treated only with cryoprecipitate and fresh frozen plasma. Professor Bloom considered it to be

"….. noteworthy that no haemophiliac patient with AIDS definitively related to transfusion of blood products from Germany, where large amounts of American Factor VIII had been used for many years, whereas the Portuguese patient with AIDS had only been treated with cryoprecipitate and fresh frozen plasma. Therefore the role of American concentrates in the causation of AIDS in European haemophiliacs must be regarded as unproven."

The article went on to state that 23 out of 135 haemophilia physicians in Europe had reduced their prescribing of American blood products, and only 7 had stopped using them altogether. Professor Bloom concluded:

"In view of the immense benefits the haemophiliacs have derived from treatment, physicians are naturally reluctant to abandon these agents, with their hypothetical dangers, in the absence of alternative concentrates which have been proven safer."

144. On 26 August 1984 the WFH Medical Board adopted resolutions to that effect in the following terms: [233]

"• Evidence is insufficient, at the present, to recommend any change in treatment. Therefore, present treatment of haemophilia should continue with whatever blood products are available, according to the judgement of the individual physician and furthermore:

• A critical need exists for data on the outcome of various viral attenuation strategies of plasma derivatives, as to the development of AIDS and Non-A, Non-B Hepatitis, and the development of side effects."

145. In August 1984, the World Federation of Haemophilia Congress took place in Rio De Janeiro, Brazil,[234] where the following presentations were given:

a. The results of the experiments undertaken by the Communicable Disease Centre (CDC) in the US to ascertain whether HTLV-III was destroyed by

[233] BART0000826_001 at p.1.

[234] It is likely that Dr Aronstam attended this conference - WITN1243001 at para 29.

heat. Bruce Everatt's report of these experiments states that the virus 'was readily destroyed by short periods of heat expsoure'.[235]

b. The results of 29 patients who had been treated with heat treated Behringwerke product for 3 years and who had not sero converted.[236]

146. On 1 November 1984 a meeting took place in Groningen in the Netherlands at which scientists from the CDC demonstrated that HTLV-III was heat sensitive and could, according to Dr Perry's evidence to the Penrose inquiry, be '*substantially inactivated at relatively low temperatures (68 degrees) in freeze dried FVIII products*'.[237]

147. On 15 – 17 April 1985 an International Conference on AIDS, sponsored by the United States Department of Health and Human Services and WHO, took place in Atlanta. This concluded and recommended that action should be taken to:

a. Inform the public that LAV/HTLV-III infection was acquired through the transfusion of contaminated blood and blood products.

b. Screen, where feasible, potential donors of blood and plasma for antibody to LAV/HTLVIII. Potential donors should be warned in advance about this screening procedure.

c. Reduce the risk of transmission of LAV/HTLV-III which might be present in concentrates of factors VIII and IX, by heat treatment or other proven methods of inactivation. [238]

148. The European Health Committee's Committee of Experts on Blood Transfusion and Immunohaematology held a meeting between 28 and 31 May 1985 at which they made some recommendations about HIV and AIDS. The main report of that meeting recorded the recommendations set out at appendix V as follows:

"Considering that the aim of the Council of Europe is to achieve greater unity between its members and that this aim may be pursued, inter alia, by the adoption of common regulations in the health field;

[235] PRSE0000831 at p.7.
[236] RLIT0001934.
[237] PRSE0002178 at p.17.
[238] SHPL0000245_013.

Considering the growing importance of a new and severe health hazard, Acquired Immune Deficiency Syndrome (AIDS), that is caused by an infectious agent transmissible by blood and blood products;

……

Recalling again the basic principles to minimise the hazard of transmissible infectious diseases by blood or blood products drawn up in the context of the work of the Committee of Experts on Blood Transfusion and Immunohaematology:

1 *to expose the recipient to a minimum number of donations of blood when the transfusion is of cellular and coagulation factor products,*

2 *to achieve national self-sufficiency in the production of coagulation factor products from voluntary, non-remunerated donors,*

3 *to avoid the importation of blood plasma and coagulation factor products from countries with risk populations and from paid donors*

Noting that all member states are taking steps to introduce screening techniques aimed at identifying the presence of serological markers of AIDS in blood donors;

Aware of the important ethical, medical and social implications of such screening;

Recommends the government of member States:

I to take all necessary steps and measures with respect to the screening of blood donors for the presence of serological markers of Acquired Immune Deficiency Syndrome, so as to ensure that:

- *donors are made aware that their blood may be tested for the presence of markers;*
- *an accurate method of evaluating the specificity of the screening test is available to confirm a positive result;*
- *adequate counselling facilities are available to any donor who is informed of abnormal serological findings;*

II to arrange for alternative sites for such testing to be established in advance of the commencement of testing in blood transfusion services, in order to avoid attracting persons to blood donations sessions whose motive is to be tested for the presence of the serological markers;

III in co-operation with the appropriate health authorities, ethical committees, blood transfusion experts and medical and donor associations, to confront,

and, as far as possible, resolve the wider ethical, social and medical issues raised by the screening of donor for the presence of serological markers of AIDS, particularly whether, when and in what way donors are to be informed of abnormal serological findings.

IV – to pursue rapid and full implementation of Recommendations No/ R(80)5, No. R(81)14 and No. R(83)8, and, notwithstanding the increasing use of screening techniques, to continue to provide all blood donors with information about the syndrome so that those in risk groups will refrain from donating."[239]

149. Appendix VIII of the report of that meeting is a report on 'AIDS Developments in Member States, Finland and Australia'.[240] The report provided as follows:
    a. A committee of experts had suggested that all donors should be tested for LAV/HTLV-III. Some blood transfusion centres had introduced the test experimentally.
    b. No decision had been made as to whether to inform blood donors found to have positive markers. [241]

150. In addition, the report set out the steps taken thus far by a variety of countries in response to the risk of AIDS. The information coming from those countries that have their own section in this report, will be set out in those sections. The information relevant to the other countries who contributed to that report is as follows:
    a. Austria - blood donation organisations were starting to test for LAV/HTLV-III antibodies.
    b. Cyprus – no AIDS cases had been reported there. There was no screening for LAV/HTLV-III. It was thought that measures to exclude homosexuals and high risk groups from donating blood would have to be introduced in the near future.
    c. Greece – blood transfusion services were being kept informed about AIDS but no information was being given to donors '*because of special considerations applying, eg, family and social problems*.' The rejection of any donor '*is handled discreetly and based on a pretext*.' Most people with haemophilia had been

[239] NHBT0009083_006.
[240] NHBT0009083_009.
[241] NHBT0009083_009.

tested for LAV/HTLV-III. There had been a pilot of screening in one blood transfusion centre. There was a committee on AIDs to which all suspected cases were reported.

d. Malta – screening blood donors for LAV/HTLV-III was intended to be introduced in the coming months following a trial comparing results in the random donor population with the country's 22 people with severe haemophilia. Efforts were being made to use heat treated product.
e. Portugal – screening programmes were starting on people with haemophilia and those under haemodialysis. The possibility of extending screening to blood donors was dependent on finances.
f. Sweden – a National AIDS group had been set up. It had been decided that testing for LAV/HTLV-III should start for at risk groups from 1 June 1985, and that all blood and blood products should be tested from 1 August 1985. Donors would not be informed of the results if positive, to avoid people coming to give blood for the purpose of being tested.
g. Switzerland – Anti-HTLV-III testing would be declared compulsory, but how to inform and counsel positive donors was to be '*studied*'.

151. In June 1985 an article was published in the Annals of Internal Medicine authored by Lederman, Ratnoff, Evatt, McDougal entitled 'Acquisition of Antibody to Lymphadenopathy - Associated Virus in Patients with Classic Haemophilia (Factor VIII Deficiency).[242] This reported that of the samples assayed from 149 patients with haemophilia:
    a. No patient samples obtained before 1980 contained the antibody to LAV.
    b. The prevalence of antibody in samples from 1980 was 15%.
    c. The prevalence of antibody in samples taken from 1984 had risen to 62%.
    d. However, none of the 8 untreated patients with haemophilia and none of the 26 people with haemophilia treated solely with cryoprecipitate had LAV antibodies.

152. The authors concluded that "*Treatment with locally prepared cryoprecipitates was not associated with serologic evidence of virus exposure.*"

[242] SHPL0000545_023.

153. A further recommendation was adopted by the Council of Europe's Committee of Ministers on 13 September 1985, on the screening of blood donors and the presence of AIDS markers.[243] Amongst the recommendations made was for Member States:

a. where they were considering, in the light of the national situation, the introduction of screening procedures for the presence of AIDS markers in blood donors, to take all the necessary steps and measures to ensure that:

i. donors were made aware that their blood may be tested for the presence of AIDS markers; and

ii. competent counselling facilities were available to any donor who was informed of abnormal serological findings;

b. to arrange for alternative sites for such testing to be established in advance of the commencement of testing in blood transfusion services, in order to avoid attracting persons to blood donations sessions whose motive was to be tested for the presence of serological markers; and

c. to establish a programme for the production of blood products, in particular coagulation factors for the treatment of haemophilia, which included suitable procedures for the inactivation of the responsible virus.

154. The UK did some research on the measures taken by other countries in response to AIDS, probably in December 1985[244] (the table setting out the research is undated but there is a letter circulating it dated 17 December 1985).[245] The information coming from those countries that have their own section in this report, will be set out in those sections. The information relevant to the other countries who contributed to that report is as follows:

a. Austria – Legislation had been enacted to ensure that all blood donations were tested. Legislation had been proposed (to come into force it was hoped early in 1986) to require: every case of AIDS to be reported; prostitutes to have regular tests and if positive would '*be forbidden to ply trade*'; doctors to inform donors if they were infected; the establishment of special laboratories for testing; and for the Ministry of Health to educate the public on all aspects of the infection. As to the last of these, an educational film had been commissioned which it was hoped would

[243] DHSC0002478_081.
[244] DHSC0002289_065.
[245] DHSC0003893_021.

be aired on National Television that winter. The non-legislative measures that had been taken were the financing of a series of centres to allow people to go for confidential testing, and a recommendation that all prisoners should be tested '*and held separately if necessary*'.

b. Cyprus – the non-legislative measures that had been taken were the universal testing of blood donors and the setting up of a committee to examine the legislation applicable in other countries.

c. Ireland – the non-legislative measures that had been taken were the surveillance and monitoring of AIDS cases on an informal basis, and education of the public and medical personnel.

d. Greece - the non-legislative measures that had been taken were the issuing of Ministry of Health circulars with instructions for doctors, hospitals and the blood transfusion service on procedures to be followed in AIDS cases; the testing of blood donations and mandatory reporting by hospitals to the Ministry of all AIDS cases.

e. Luxembourg – the non-legislative measures that had been taken were the mandatory testing of blood donations since 1 August 1985; the mandatory reporting of confirmed AIDS cases and '*any clinical signs of AIDS'* by the medical profession to the Chief Inspector of Public Health; and the issue of booklets to clinicians advising them about what to look for and how to respond. There were plans for the issue of a booklet to the public informing them about AIDS. It would include the details of an organisation that would help them anonymously.

f. Malta had enacted legislation to give powers to: enter the house of anyone either infected with AIDS or having had contact with AIDS; suspend that person from work for 10 weeks if there was a suspicion (s)he might spread AIDS; require anyone either with AIDS or who had been exposed to it, to isolate or be given (free) treatment until it was no longer necessary; and to require anyone whose occupation was capable of spreading the disease to have periodic tests and medical examinations.

g. Switzerland – the non-legislative measure that had been taken was to disqualify anyone with AIDS symptoms from the Armed Forces.

h. Los Angeles City had enacted legislation to prohibit discrimination against someone with AIDS.

155. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[246] The information provided includes information on prevalence, screening for HIV, arrangements for the counselling of donors, follow-up of patients and alternative testing sites, treatment provided to people with haemophilia. The information given by the individual countries appears in their individual sections. Dr Gunson also provided some general information:

a. The total number of AIDS patients recorded between December 1985 and April 1986 was 2,336. The number of deaths were 1,207.

b. The positive rates for patients with haemophilia A varied considerably from 4% in Belgium and 8% in Norway, to over 90% in Malta and the USA. Dr Gunson surmised that *"The low rate of positivity in Belgium and Norway could probably be attributed to the almost exclusive use of cryoprecipitate prepared from local donors."*

c. Dr Gunson's report went on: *"With a few exceptions the positive anti-HTLV 3/LAV rate for patients with Haemophilia A was greater than that for Haemophilia B and the incidence of AIDS and AIDS related complex was also higher in most instances. Dr A FARRUGIA (Malta) commented that the 95% incidence of anti-HTLV3/LAV antibodies in Haemophilia A patients in Malta had almost certainly arisen because these patients had been exclusively treated with imported Factor VIII concentrate, whilst the patients with Haemophilia B had been treated with Factor IX concentrate obtained from European voluntary donors.*

It was evident that where cryoprecipitate was used predominantly to treat Haemophilia A that the incidence of anti-HTLV 3/LAV was low. The apparent discrepancy in France was explained by Dr B GENETET who said that school children with Haemophilia A are given cryoprecipitate during term but imported Factor VIII concentrate during the school holidays."

[246] PRSE0003860.

Sample countries: Knowledge of, and response to, HIV/AIDS

Netherlands

156. The Krever report has a section on the knowledge of the risk of HTLV-III and the response to it in the Netherlands which is the source for much of what is set out below.[247]

Knowledge of risk and treatment policies

157. The first report of a patient with AIDS in the Netherlands was at the Rotterdam University Hospital symposium in May 1982.

158. On 20 July 1982 there was an article in the Dutch National newspaper, de Volkskrant which made the link between AIDS and blood. [248]

159. As a result of growing concern in the USA and a visit to the CDC in Atlanta in 1982, the executive board of the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service (CLB) met with the Haemophilia Society, specialist physicians, and the government in November 1982. At that meeting:
    a. An emergency plan was formulated to increase the production of small pool cryoprecipitate as it was considered safer than Factor VIII concentrate, although this did not eliminate the use of Factor VIII concentrate.
    b. A decision was made to start a clinical trial in Dutch people with haemophilia to determine whether there were any immune changes and, if so, the nature and incidence of the reported immune changes after treatment with various clotting factor concentrates and cryoprecipitate. [249]

160. By January 1983 agreement had been reached between CLB, treating physicians, the Dutch Association of Haemophilia Patients and the National Institute for Public Health and Environmental Protection about steps that should be taken to reduce the risk of

[247] KREV0000001 at pp.906-928.
[248] **WITN6411008.**
[249] CBLA0000058_036 at p.17.

transmission of HTLV-III.[250] These were:

a. To use cryoprecipitate wherever possible.
b. To treat new patients and children under the age of four with cryoprecipitate exclusively.
c. To treat patients with moderately severe or mild haemophilia A with DDAVP, or if necessary, cryoprecipitate.
d. To use domestically produced Factor VIII concentrates when concentrates were necessary.
e. To use imported Factor VIII concentrates only for patients with severe allergic reaction or haemolytic reactions to Dutch products.
f. To treat type B people with haemophilia with domestically produced Factor IX products.[251]

161. On 27 February 1983 the Dutch Association of Haemophilia Patients wrote to members to alert them that it was highly likely that American people with haemophilia had been infected by HIV from infected donors by using factor concentrates.[252]

162. In April 1983 the Director General of the Netherlands National Institute of Public Health and Environmental Protection wrote to the Minister of Health to say that experts generally agreed that U.S. factor concentrates should not be used. He recommended that the use of imported Factor VIII concentrate made from plasma from paid donors should be prohibited until further notice. Physicians of people with haemophilia who had signed a consent were exempt.[253]

163. Also in April 1983, treating physicians attended a highly publicised one day symposium on AIDS organised by the Red Cross Central Laboratory, at which the preliminary results from the first study of T-cell rations in Dutch people with haemophilia were presented. These showed that the rations of those treated with imported Factor VIII concentrate were often abnormal.[254]

[250] KREV0000001 at p.922; LCAN0000018_101; CBLA0000058_036 at p.18.
[251] This agreement was formulated as guidelines and published in May 1983 in the Dutch Medical Journal and in the magazine "Factor" which was distributed among members of the haemophilia foundation in the Netherlands.
[252] KREV0000001 at p.923.
[253] KREV0000001 at p.915.
[254] KREV0000001 at p.924.

164. According to Professor Cees Th. Smit Sibinga (Managing Director of the Red Cross Blood Bank in Groningen 1976 – 2001), up until the second half of the 1980s when heat treated products became available, cryoprecipitate was preferred to concentrate by the haemophilia treaters because of its traceability. [255]

165. According to the expert evidence of Professor van Aken given to the Penrose Inquiry, there was one blood bank in the Netherlands (unnamed) which used a different policy: *"here the use of commercial heat-treated factors VIII concentrate was recommended and such products were distributed. The other blood banks prepared and supplied only cryoprecipitate."*[256]

166. An article published in the BMJ on 19 April 1986 reported on the rate of seroconversion of a group of 18 Dutch people with severe haemophilia who had been treated prior to June 1983 with non-heat treated American concentrates, and had a '*remarkably low*' prevalence of HTLV-III (5%) compared with other groups in the USA and Europe which ranged from 53% to 94%.[257] No patients sero-converted after moving to heat treated product. It also cited unpublished research by C Breederveld, which found that from 1983 to 1985 seroconversion for HTLV-III occurred in 27% of Dutch people with haemophilia who were treated with a local non-heat treated concentrate.

167. In a later article published in Transfusion in 1987 by Daehen et al, it was reported that of 17 adults with severe haemophilia A who were treated with heat treated Factor VIII concentrate only one tested positive for HIV: *"The prevalence of HIV positivity in our patients was very low (5.9%) in comparison to that in other groups from the United States and Europe. This was probably due to the coincidental use of batches of factor VIII concentrate that had been collected before 1981, when the prevalence of HIV infection, and thus contamination of donor pools, was much lower."*[258]

168. In an article from 1988, a national multicentre study to investigate the effects of donor

[255] WITN6412001 at para 13.
[256] PRSE0000554 at p.3.
[257] PRSE0003114.
[258] SHPL0000511_035.

selection and the use of heat-treated plasma products on seroconversion to HIV in 157 Dutch people with haemophilia was reported.[259] All patients included in the study were seronegative for HIV antibodies in 1983. Thirteen percent (20/157) seroconverted between 1983 and 1986. Nineteen of 20 seroconversions could be related to the use of non heat-treated products in the year preceding HIV antibody seroconversion. One seroconversion occurred in a person using heat-treated non donor screened product.

169. In 1993 the Ombudsman undertook an investigation into the central Government's role into the infection with HIV of people with haemophilia, triggered by a complaint from the Netherlands Haemophilia Society. The report was made public in July 1995. This report found that by 1983 it had become clear that the risk of HIV infection was higher with Factor VIII concentrate than with cryoprecipitate, and that the non-heat treated American products posed a greater threat of infection than the non-heat treated Dutch products. The Ombudsman however concluded that the Government's decision to continue to permit the use of imported products was understandable.[260] Nevertheless, the Ombudsman did find improper conduct in the following respects:

    a. The absence of an initiative in late 1984/early 1985 to reduce the risk of infection from the use of domestic non-heat treated blood concentrates.
    b. The failure to require Dutch blood banks and manufacturers to heat blood concentrates until January 1988.
    c. The failure to recall Armour Factor VIII concentrates before the beginning of 1988.

Donor selection

170. At a meeting on 30 January 1983, the CBL deferred making a decision about excluding male homosexuals from donating, instead agreeing to examine ways in which donors at risk could be educated about AIDS.[261] This led to a series of meetings between different interest groups, culminating in an agreement in April 1983 that male homosexuals would not be barred from donating, but blood banks and homosexual organisations would launch an information campaign to promote self-exclusions by gay men with multiple

[259] RLIT0001938.
[260] KREV0000001 at p.921.
[261] KREV0000001 at p.913.

partners.[262] A brochure asking high-risk donors to self-exclude was introduced at some point between April and June 1983.[263] It advised members of high risk groups to consider not donating blood.[264]

171. In the information given to the Committee of Experts on Blood Transfusion and Immunohaematology for their meeting in May 1983, the Netherlands said as follows:

"No actual measures with regard to the selection of donors have so far been suggested, let alone taken. It is a very difficult and delicate problem.

….. In the Netherlands, it is felt that the only possible measure to take would be to write a pamphlet explaining the great dangers of this disease and describing the donor populations who are a possible source of the causing agent of this disease – if indeed there is such an agent; it would be left to the individual donor to decide whether he/she is willing to withdraw from the donor panel.

…… there is of course the one concerning the use of plasma products from areas in which the disease has manifested itself (eg, the USA). Although no official measures have been taken in the Netherlands, the clinicians, for example, those responsible for the treatment of haemophiliacs, have requested that no Factor VIII concentrate from the United States should be used in future."[265]

172. In his statement to the Inquiry, Professor Sibinga gives an account of how donor selection worked in the centre he ran in Groningen.[266]

"In 1984 we started with focused donor information on the risks of HIV transmission and personal risk behaviour. The donor questionnaire was redesigned with a series of risk behaviour questions, donor attendants were trained, and donors were motivated to confidentially self-exclude."

Products and viral inactivation

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[262] KREV0000001 at p.913.
[263] CBLA0000058_036 at p.18; LCAN0000018_101.
[264] KREV0000001 at p.914.
[265] DHSC0000717.
[266] WITN6412001 at para 19.

173. The CLB first received circumstantial evidence that the yet to be identified AIDS agent might be heat sensitive in 1983, following the publication of Montagnier's article in the Science journal in which he announced he had isolated the virus. The implications of these findings were discussed at CLB and the organisation was aware that retroviruses were generally sensitive to heat.

174. In late April or early May 1983, Travenol made its heat treated Factor VIII concentrate (Hemofil-T) available to Dutch physicians. Travenol was formally licensed to import Hemofil-T into the Netherlands in August 1983.[267]

175. Further licences to import heat treated product followed: for Tramedico (spring 1984); and various other companies in 1986.[268]

176. In the summer of 1984 CBL held discussions with Baxter/Travenol concerning the possibility of obtaining a licence from Baxter to manufacture heat treated Factor VIII concentrate using the process developed by Baxter. This was agreed at the end of 1984.[269]

177. As noted above, in February 1985 the Dutch started to make freeze-dried cryoprecipitate from two rather than four donations.[270]

178. In April 1985, domestic heat-treated Factor VIII concentrate was given to patients without transmission of virus. CBL announced that as of 3 June 1985 it would only supply heat treated products. CBL did not distribute non-heat treated Factor VIII concentrates after this date. Hospitals were able to replace their non-heat treated stock with heat treated product.[271]

179. From 3 June 1985 CBL began testing cryoprecipitate, still in stock, for HTLV-III before distributing it.[272]

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[267] KREV0000001 at p.914.
[268] KREV0000001 at pp.914-915.
[269] KREV0000001 at p.915.
[270] BAYP0000022_050 at p.9 – a letter from van der Meer in Vox Sang, 22, 554 – 565 (1972) 'International Forum' at p.561 describes how the Netherlands Red Cross Blood Transfusion Service made freeze dried cryoprecipitate out of four pooled donations. LCAN0000018_101.
[271] KREV0000001 at p.916.
[272] LCAN0000018_101.

180. From 22 July 1985 CBL only supplied heat treated Factor IX concentrate. Any non-heat treated product produced after 1 June 1985 could be exchanged for heat-treated product until the beginning of February 1996.[273]

181. In December 1985, CBL began heat-treating cryoprecipitate. This was clinically evaluated in paediatric patients in 1988 and 1989.[274]

182. The regional blood banks, however, did not take to heat treating at the same time as CBL, and were not required to until 1 January 1988 when regulations requiring the use of viral inactivation in the production of Factor VIII concentrate and cryoprecipitate came into force. The Ombudsman, in the investigation published in 1995, found that the failure to forbid the use of unheated product at the end of 1984 was negligent.[275]

183. In 1990 the Government ordered a stop to cryoprecipitate production and treatment for precautionary reasons.[276]

Donation screening

184. Surrogate testing was not introduced in the Netherlands. It was considered by CBL before the anti-HIV test kits were available but experience was that the surrogate tests in the USA indicated low sensitivity and specificity and were not suitable for screening blood donations. [277]

185. The first experimental test kits for HIV were available in the Netherlands in November 1984. In the last part of 1984 and the beginning of 1985 the CBL performed a comparative study of several anti-HIV test kits to determine sensitivity and specificity.[278]

186. The Abbott test kits became commercially available in the Netherlands on 1 April 1985.[279] The routine screening for antibodies to HIV in the plasma of donors who

[273] KREV0000001 at p.916.
[274] KREV0000001 at p.916; WITN6412001 at para 31.
[275] KREV0000001 at p.917.
[276] WITN6412001 at para 17.
[277] CBLA0000058_036 at p.27.
[278] CBLA0000058_036.
[279] KREV0000001 at p.917.

attended the mobile CBL donation points began in March 1985. By either June or July 1985 routine screening of all donations had been introduced. Initially, donors were not informed that testing was performed and seropositive donors were not informed of the results. This decision was taken on the basis that as alternative (community) testing facilities for non-donors were not yet in place there was a risk that those from high risk groups would give blood in order to get tested.

187. The community testing sites were established by December 1985 and from the beginning of 1986 any donor who tested positive had to be told about their result by a physician in a personal interview and in writing, with the donor being referred for further help and support to another physician. The results would only be passed on to the donor's GP with the donor's express consent.[280]

188. CBL began confirmatory testing using the Western Blot technique in January 1986.[281]

189. By May 1986, the Netherlands had screened 350,000 donations. 10 had tested positive (0.003%). They used the ELISA direct and the ELISA competitive screening test, with the Western Blot and unspecified other tests as confirmatory tests.[282]

Prevalence

190. The Krever report states that the first AIDS case in the Netherlands was in the autumn of 1981. By 1982 there were five cases of AIDS. In 1983 there were 31 cases, 67 by 1985 and 136 by 1986.[283]

191. The figures in the draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, are rather different. This says that by 20 October 1983 the Netherlands had reported 12 cases of AIDs to the WHO. The Netherlands reported the number of cases under each "Year of Diagnosis" as 1982 (3) and 1983 (9).[284]

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[280] CBLA0000058_036 at pp.28-29; KREV0000001 at p.919.
[281] KREV0000001 at p.920.
[282] PRSE0003860.
[283] KREV0000001 at p.911.
[284] CBLA0001775 at p.35.

192. In January 1985, the Red Cross Central Laboratory used a non-licensed experimental technique to conduct a sero-prevalence study using blood collected from Dutch haemophilia patients in 1983 and 1984. Those who had been given imported concentrate exhibited an HIV infection rate of 35% (14/40). Those who had received a mixture of both Dutch cryoprecipitate and Dutch concentrate exhibited an HIV infection rate of 10% (2/20), whereas those who had only been given cryoprecipitate exhibited a rate of 3.6% (2/56).[285]

193. According to a study by the Netherlands Government completed in July 1995, between 1979 and 1985 approximately 150 transfused patients and 170 people with haemophilia (13% of the Dutch people with haemophilia) were infected with HIV.[286]

194. The first report of AIDS among people with haemophilia came in 1987. Three patients were diagnosed that year, 5 in 1988 and 6 in 1989.[287]

195. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, 20 people with haemophilia and 28 transfusion recipients were reported as having AIDs in the Netherlands.[288]

196. In 1991, an academic article in *Oncology News* reported that the Netherlands had an HIV infection rate of 17% amongst patients with haemophilia.[289] It is worth noting that Dr Elizabeth Mayne in the expert report she prepared for the HIV litigation, compared this 17% infection rate in the Netherlands with that of the UK asking *'If the Department of Health had provided further financial support at an earlier time, would this have accrued significant patient benefit? The reply is probably in the affirmative. For example, in the Netherlands, an overall 17% positivity for HIV infection in 1250 Haemophiliacs was achieved;*

[285] KREV0000001 at p.924.
[286] KREV0000001 at p.910.
[287] KREV0000001 at p.911.
[288] NHBT0010038_001 at p.25.
[289] MACK0000192_004 at p.2.
[290] CBLA0000072_024 p. 25.

95% of the blood product used was obtained from domestic volunteer donors.' [290]

197. According to the European Centre for the Epidemiologial Monitoring of AIDS, as at 31 December 1996 there were 62 people with haemophilia with AIDS in the Netherlands (1.5% of all AIDS cases) and 39 transfusion recipients with AIDS (0.9%).[291]

Germany

198. This section is concerned with events in what was, in the 1980s, West Germany.

199. The Krever report has a useful section on the German response to HIV and AIDS in the 1980s.[292] This explains that during the 1980s the Robert Koch Institute in Berlin monitored outbreaks of disease and conducted disease surveillance. It collected data on AIDS.

200. There have been various investigations into infected blood in Germany:
    a. In November 1992 the Health Committee of the German Parliament produced a report 'On the risk of HIV Infection through Blood Products'.[293]
    b. In October 1993 that same committee produced a second report.[294]
    c. On 29 October 1993 the Third Investigation Committee was established to examine the role of the federal government in the transmission of HIV through blood and blood products. It produced an interim report on 31 January 1994 and a final report at the end of October 1994.[295]

Knowledge of risk

201. According to the Krever report,[296] in November 1982 an epidemiologist from the German national institute for infectious diseases (Dr L'age-Stehr, of the Robert Koch Institute in Berlin) visited the AIDS task force at the Center for Disease Control (CDC)

[290] CBLA0000072_024 p. 25.
[291] As cited in KREV0000001 at p. 910.
[292] KREV0000001 at pp.850-884.
[293] KREV0000001 at p. 853.
[294] KREV0000001 at p. 854.
[295] RLIT0001934.
[296] KREV0000001 at p.855.

in the USA. She reported in the Federal Health Bulletin – the Bundesgesundheitsblatt - that AIDS appeared to be caused by an unknown infectious agent transmitted through blood and blood products. Her report was reprinted in the German Medical Gazette (Deutsches Arzteblatt) on 18 Feb 1983 and distributed to all physicians.

202. The Krever report also records that the Investigation Committee (established by the speaker of the German parliament on 29 October 1993 to examine the role of the federal government in the transmission of HIV through blood and blood products) found that:

"...although the first haemophilia AIDS case in Germany was reported to Dr L'age-Stehr at the Robert Koch institute in April 1983 a diagnosis of PML and a lack of cooperation on the part of the treating physicians impeded the investigation of the case, and the ensuing delay in confirming the case enabled physicians and the pharmaceutical industry to deny the existence of AIDS in Germany. It concluded that the treating physician should have known in June 1983 that the Bonn case in May 1982 was the first fatal AIDS case in a German haemophiliac ..... The Investigation Committee also found that by the end of 1983 there had been several haemophilia AIDS cases in Germany that were not reported to the Federal Health Office. The committee stated that the facts demonstrate that physicians treating haemophilia patients at that time either knowingly disregarded, or simply did not recognize, concrete indications of HIV infections in their patients."[297]

203. In 1982, the Federal Health Office had set up an AIDS working group.[298] The Federal Health Office published guidelines in June 1985 entitled 'Standardization of Use of Factor VIII and Factor IX Concentrate'. These guidelines described the risk of AIDS being transmitted via clotting factors to be 'very low'.[299]

Donor selection measures

204. In January 1983 Germany's Red Cross added questions in their donor questionnaire to elicit information about whether the donor had suffered the early symptoms of AIDS,

[297] KREV0000001 at pp.856-857.

[298] PRSE0004082 at p.2.

[299] RLIT0000456 at p.211 and Bundesgesundheitsamt, ed. *Klinik und Therapie der Haemophilie A und B. Indikation und Therapie mit Faktor VIII-und IX-Kozentraten* [Clinical course and treatment of haemophilia A and B. Indication and therapy with Factor VIII and Factor IX concentrates] Fundesgesundheitsblatt 28 (6 June 1985).

such as weight loss, night sweats, dry coughing, diarrhoea, and lymph node swellings. Anyone exhibiting those symptoms was excluded from donating. [300]

205. In June 1983 most Red Cross centres started to exclude people from high risk groups, including intravenous drug users and homosexual men, from blood donation. Other blood banks followed.[301]

206. On 6 September 1983 the Federal Health Office issued a press release stating that all blood donors must be informed of the AIDS virus, and that those in high risk groups should be asked to self-exclude.[302] As of September 1983, donors were provided with a leaflet about AIDS which set out who was at the highest risk of infection, and what the symptoms of the disease were.[303]

207. By May 1985, information about AIDS was being provided to donors, who were obliged to sign a form to the effect that they had read and understood the information and did not belong to any of the high risk groups. [304]

208. In July 1987 confidential self-exclusion procedures were made mandatory in West Germany.[305]

209. In July 1988 the Federal Health Office wrote to manufacturers informing them of its intention to impose mandatory direct questioning on donors about their sexual contact with West Africans.[306] On 11 December 1988, the Federal Health Office announced that effective immediately, all donors who had had sexual contact with West Africans or their sexual partners were to be excluded from donation.

210. In February 1992, Dr Gunson made enquiries with other countries about their donor leaflets '*to ensure that donors with high risk activities which may give an increased risk of HIV do not donate blood.*'[307] He received a copy of the letter sent to German donors.

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[300] RLIT0000456 at p.214 also KREV0000001 at p.862.
[301] RLIT0000456 at p.214.
[302] KREV0000001 at p.863.
[303] KREV0000001 at p.863.
[304] As set out in the European Health Committee Report on AIDS Developments in Member States, Finland and Australia dated 28 to 31 May 1985. NHBT0009083_009.
[305] RLIT0000456 at p.214.
[306] KREV0000001 at p.863.
[307] NHBT0007305_001.

211. [308] Dr Gunson noted that this letter was regional not national. A section of the letter asked the donor to make a statement, under oath, that (s)he did not belong to a risk group. Risk groups were defined as drug addicts, homosexuals, people returning from tropical countries (within the last 12 months) or someone who had had sexual contact with an infected African or their partner.

Measures with respect to the products

212. In June 1983 there was a round table meeting of clinicians in Frankfurt to discuss AIDS. It was thought that heat treatment could be efficacious against AIDS.

213. Professor Egli in a memo dated 20 June 1983 delivered to the Third Investigation Committee, recalled a discussion the University of Bonn with the Health Insurance services on 15 June 1983 at the BdO as follows:

'Dr Brackmann then stated…. In general severe hepatitis risks can be reduced by the use of the HT products, however the use of these products can also be viewed in relation to the problem of treating the AIDS syndrome in recent months. HT preparations should be used expediently in order to prevent the AIDS disease, as this disorder (particularly dangerous for the haemophiliac) has up to now been fatal in almost all cases.' [309]

214. In July 1983 a circular for patients at the Bonn Haemophilia Centre was produced. This provided at page 3:

'This clotting concentrate is heated to high temperatures and it is assumed that this process does not only eradicate the hepatitis pathogen, but also other possible disease pathogens. If AIDS can in fact be transmitted through plasma products, then it is to be hoped that the risk of AIDS can possibly be obliterated or even entirely eliminated by these products.' [310]

215. According to the Krever report, a meeting took place on 14 November 1983 which was attended by representatives from pharmaceutical companies, the Red Cross, hospitals

[308] NHBT0007305_003 at pp.7-8.

[309] RLIT0001934 at p.67.

[310] RLIT0001934 at p.67.

and representatives of the Federal association of the pharmaceutical industry ("BPI").[311] There was discussion of a range of measures that could be implemented to guard against the risk of AIDS. These included the introduction of mandatory hepatitis B core testing, banning imported product, restricting treatment to cryoprecipitate only, treating people with haemophilia solely with heat treated product, batch testing of plasma, restricting pool sizes to 6,000 donors, the introduction of donor screening guidelines and the introduction of mandatory reporting of AIDS cases. No consensus about the introduction of any of these measures could be reached.

216. On 8 June 1984 the Federal Health Office issued an Order which provided that:
    a. Manufacturers of blood products were required to identify the country of origin of the plasma in their product, where the product was manufactured, the size of the donor pool, the process of donor selection and give a warning regarding the possible transmission of NANB and AIDS.
    b. Manufacturers were prohibited from mixing plasma from different countries.
    c. Plasma was to be tested for syphilis, hepatitis B Core antigen and surface antigen and either glutamate pyruvate transaminase (GPT) or ALT from 1 January 1985.[312]

217. There was significant objection to the June 1984 Order by the Red Cross and many blood product manufacturers. As a result of this, the Order was amended in December 1984:
    a. The provisions requiring the identification of the country of origin of the plasma, batch testing and the prohibition against mixing of plasma from different countries were dropped.
    b. Anti-core testing was only required in the absence of HIV testing, which had to be implemented by 1 July 1985. This date was then extended in February 1985 until October 1985.[313]
    c. Information had to be given as to whether and if so how, the product had been virally inactivated, to be implemented by 1 March 1985.
    d. Imported factor concentrates could be used as long as the donor screening guidelines of the country of origin had been observed.[314]

[311] KREV0000001 at p.859 – which account is supported by RLIT0000456.
[312] KREV0000001 at p.860; RLIT0000456 at pp.215 and 216.
[313] KREV0000001 at p.869.
[314] KREV0000001 at p.861.

218. There then followed publication of a number of papers in medical journals reviewing the efficacy and safety of heat treated Factor VIII including:

a. In May 1985, the report of a study of 113 German PWH published in the Lancet which showed that patients using only heat-treated concentrates did not become infected with the AIDS virus. The authors of that paper concluded that it seemed "*quite reasonable to treat previously unexposed haemophiliacs with heat-treated concentrates only.*" [315]

b. Professor Egli, with others (Wernet, Schneider, Brackmann et al.), presented a long term study at a round table discussion in October 1984 titled 'Striking absence of LAV 1 antibodies after exclusive use of heat-treated Factor FVIII Concentrates'.[316] According to this, clinical studies with heat treated Factor VIII involving 29 patients had been running for more than three years and – as tested at the Pasteur Institute in July 1984 and reported for the first time at the World Federation of Haemophilia Congress in Rio de Janiero in August 1984 – none of them had LAV antibodies.[317]

219. According to the Krever report, the German blood product manufacturers informed the Federal Health Office that as of 1 October 1985 they would only be distributing heat treated Factor VIII concentrate.[318] However, as non-heat treated products were not recalled, they were still being distributed as late as 1987.[319]

220. Regulations came into force on 11 December 1988 requiring Factor VIII to be virally inactivated. These regulations were declared invalid by the Berlin Higher Administrative Court in July 1990.[320]

Screening of donations

[315] CBLA0000061_049.
[316] Published later in 1986 RLIT0001935.
[317] RLIT0001934 at p.68. Bruce Evatt of CDC also presented the study at Rio that showed that HLTV-III was destroyed by heat: CVHB0000042.
[318] KREV0000001 at p.866; PRSE0004082 at p.2-3.
[319] KREV0000001 at p.867.
[320] KREV0000001 at p.867.

221. In November 1984, sera were sampled in six major West German blood banks in order to evaluate the risk of transmission of HTLV-III from the donor population. The results were written up in the Lancet in February 1985.[321] 6,720 samples were tested. 0.16% of those samples had antibodies to HTLV-III and '*were probably infected*'. The authors therefore concluded that '*The risk of infection with HTLV-III for the individual blood transfusion recipient justifies the testing of blood donors for HTLV-III.*'

222. Screening for the majority of blood donations was introduced in the spring of 1985. It did not however become compulsory until 1 October 1985.[322] Blood that was already in circulation was neither tested nor withdrawn.[323]

223. The European Health Committee produced a Report on AIDS Developments in Member States, Finland and Australia, to accompany its main Meeting Report dated 28-31 May 1985. [324] This provided that in Germany, donors who were found to be positive were asked for a second specimen. This process could take up to 6 months. If the result was confirmed, the donor would be informed through his/her physician.

224. Information given by Germany to the Committee of Experts on Blood Transfusion and Immunohaematology in May 1986 about donor screening stated that:
    a. Germany began screening donations for HTLV-III in October 1995 and by May 1986, had screened one million donations. One hundred and seven donors (or 0.01%) had tested positive.
    b. They used both the ELISA Direct and Competitive tests as the screening test, with the ELISA, Western Blot and other unspecified tests as the confirmation tests.
    c. In order to stop high risk donors from donating, a leaflet was given to each donor before donating.
    d. In the event that a donor tested positive for HTLV-III, (s)he would be seen at the Medical AIDS centre.
    e. There were anonymous community testing sites available to discourage those at high risk of AIDS donating in order to be tested. [325]

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[321] NHBT0114431.
[322] NHBT0009083_009; PRSE0004082 at p.3.
[323] RLIT0000456 at p.215.
[324] NHBT0009083_009.
[325] PRSE0003860.

Use of factor products

225. In July 1983, a circular was issued for patients at the Bonn centre. Page 3 of that circular provided:

> *This factor concentrate is heated to high temperatures and it is believed that this not only eradicates hepatitis but also other pathogens present. If AIDS is in fact transmitted through plasma products, it is hoped that these products will mean the risk of AIDS can potentially be reduced or even entirely eradicated.*[326]

226. It appears from the paper entitled 'Assessment of LAV1 Antibodies in Haemophilia patients with Distinct Types of Factor VIII Substitution: Striking Absence of LAV1 Antibodies After Exclusive Use of Heat-Treated Factor VIII Concentrates'[327] that from 1983, 164 patients at the Bonn centre were treated with heat treated product, of those 29 were treated exclusively with such product. The results showed that of the 164 patients:

   a. 109 of them had been treated with conventional factor products over the last four years. In this group there were 71 (or 65%) who tested positive for LAV.
   b. There was a second group of 26 who had been treated with heat treated product in the last 6 to 24 months. Of them, 10 (38%) were LAV positive.
   c. Of the 29 treated exclusively with heat treated products, none tested positive for LAV.

227. In the order issued on 8 June 1984 by the Federal Health Office, there was a provision that factor concentrates were only to be used for the treatment of severe haemophilia.[328] As set out above, this order was the subject of much criticism, including on the basis that this provision interfered with the therapeutic freedom of doctors. The modified order issued in December 1984 no longer limited the use of Factor VIII to people with severe haemophilia.[329]

228. By May 1986:

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[326] RLIT0001934 at p.67.
[327] RLIT0001935.
[328] KREV0000001 at p.860; RLIT0000456 at pp.215 and 216.
[329] RLIT0000456 at p.216.

a. 10% of the total treatment with Factor VIII in Germany was provided by cryoprecipitate. There do not appear to have been any patients who were solely treated with cryoprecipitate.
b. 90% of the Factor VIII and Factor IX concentrate used in Germany was purchased from commercial sources.
c. The imported product did not indicate the country of origin of the donated plasma.[330]

Reporting cases of AIDS

229. The UK research, probably in December 1985, indicated that in Germany, compulsory notification of the disease had not been introduced, but federal law allowed all necessary measures to be taken. [331]

230. According to the Krever report, reporting of AIDS cases remained voluntary in Germany, although it became mandatory in September 1987 to report HIV infections.[332]

Prevalence

231. In a memorandum of the Council of Europe Committee on Blood transfusion and Immunohaematology dated April 1983 for their meeting in May 1983, it was recorded that Germany had 18 cases of AIDS, of which 2 were patients with haemophilia.[333]

232. According to a draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, by 20 October 1983 Germany had reported 3 cases of AIDs to the WHO. Germany reported the number of cases under each "Year of Diagnosis" as prior to 1979 (1) and (2) in 1983.[334]

233. In December 1983, the AIDS working Group of the Federal Health Office (Bundesgesundheitsamt) wrote a letter in the Lancet stating that since 1982 the Federal

[330] According to information given by Germany to the Committee of Experts on Blood Transfusion and Immunohaematology PRSE0003860.
[331] DHSC0002289_065; DHSC0003893_021.
[332] KREV0000001 at p.860.
[333] DHSC0000717.
[334] CBLA0001775 at p.35.

Health Office had been collecting reports of AIDS in the Federal Republic of Germany.[335] As AIDS was not a notifiable disease, all information was submitted voluntarily by the clinicians. 44 cases had been registered and 14 patients had died. Of those, one was a person with haemophilia who died in 1982. The letter went on to state:

"Cases with unexplained lymphadenopathy, fever, weight loss, malaise, and laboratory-proven dysfunction of cellular immunity, mainly in homosexual males, have also been brought to our attention. The number of such cases in West Germany is estimated to be 5 -10 times higher than the number of full-blown AIDS cases."

234. By 10 September 1985 there were 265 cases of AIDS in Germany, of whom 109 had died. Of these, 21 were people with haemophilia (although one of those had other risk factors, namely being a homosexual and drug dependant).[336]

235. In May 1986, Germany reported to the Council of Europe that:[337]
    a. As at February 1986 it had a population of 61 million, and had had 418 cases of AIDS, of whom 207 had died. Of those 10 had been infected via blood transfusion (excluding people with haemophilia).
    b. Of the 6,000 haemophilia patients in West Germany with haemophilia A and B, 2,000 received regular treatment. 99% of patients were tested for HIV, and 33% of these patients were HIV positive.

236. According to a paper published in the BMJ on 9 December 1995, between 1985 and 1993, there were 688 AIDS cases associated with blood and blood products reported in Germany.[338] Of those, 431 were people with haemophilia and 257 were transfusion recipients.

237. It appears that as at 31 March 1997, there were 529 haemophilia associated cases and 276 linked to blood transfusions.[339]

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[335] RLIT0000279.
[336] PRSE0004082 at p.6.
[337] PRSE0003860.
[338] DHSC0004556_067 at p.2, Table 2.
[339] RLIT0000456 at p.213.

238. Only since 1987 had the law required reporting of positive HIV tests to the Robert Koch-Institute. Data gathered from 1987 to 1995 indicates that 50-75% of people with haemophilia who received treatment with coagulation factor were infected with HIV.[340]

239. According to a draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, by 20 October 1983 Germany had reported 42 cases of AIDs to the WHO. Germany reported the number of cases under each "Year of Diagnosis" as prior to 1979 (1), 1979 (1), 1982 (7) and 1983 (33).[341]

240. Drawing this all together the figures look as follows:

a. Prior to 1979 West Germany had one case of AIDS.
b. In 1979 there was one case of AIDS.
c. In 1982, 7 cases were diagnosed, giving a total of 9 cases of AIDS. One of these was a person with haemophilia.
d. In 1983 there were 33 cases of AIDS, making a total of 42 cases.
e. By July 1984 there were 79 cases of AIDS.
f. By May 1985 there were 180 cases of AIDS.
g. By September 1985 there were 265 cases of AIDS, of which 20 were people with haemophilia.
h. By February 1986 there were 480 cases of AIDS, of which 10 were from blood transfusions. There were also, by this time, 2,000 people with haemophilia who had HIV.
i. By September 1990 there were 5,266 cases of AIDS and this had risen to 5,380 by November.
j. By September 1992 there were 358 people with haemophilia with AIDS and 174 transfusion recipients. By 1993 these figures had risen to 431 and 257 respectively.

[340] This is supported by the Krever report, who concluded that half of the 6,000 people with haemophilia in Germany were infected with HIV- KREV0000001 at p.853.
[341] CBLA0001775 at p.35.

k. By March 1997 these numbers had increased to 529 people with haemophilia with AIDS and 276 infected via transfusion with AIDS. .

Belgium

241. In the information provided to the Committee of Experts on Blood Transfusion and Immunohaematology for the meeting in May 1983 Belgium envisaged the temporary rejection of blood and plasma donors displaying unexpected rise in temperature, loss of weight or abnormal adenopathies who injected intravenously or had spent time in Equatorial Africa or the West Indies during the preceding three years, or had been in intimate contact with someone who had done so.[342]

242. The European Health Committee produced a Report on AIDS Developments in Member States, Finland and Australia, to accompany its main Meeting Report dated 28-31 May 1985.[343] This provided that in Belgium:

    i. They had been using a donor questionnaire which required the donor to certify that (s)he did not belong to a risk group.

    ii. Serological screening of plasmapheresis donors was to be carried out at least four times a year and that only tested plasma from regular donors would be used in the preparation of coagulation factors.

    iii. Positive results would not be passed on immediately.

243. The UK's research in December 1985 on the measures taken by various countries states that:

    a. Belgium enacted legislation requiring Belgian donor centres, which were all privately owned, to carry out a test on all donated blood to detect AIDS virus antibodies, using the Elisa method.

    b. The donor was to be informed if the results were positive.

    c. Donors were also to be informed which groups of the population were at risk.

    d. Donor centres using blood from more than 20 donors to make up a particular stock of plasma were obliged to inform the Institute of Hygiene and Epidemiology.

[342] DHSC0000717.
[343] NHBT0009083_009.

e. As of 26 September 1985, all blood donor centres were to receive state subsidies if they conformed to the relevant requirements. [344]

244. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[345] The information provided by Belgium as to its response to the risk of HLTV-III is as follows:

a. Screening of blood donations began in August 1985. By the time of the report, they had screened 283,895 donations. 15 had tested positive (0.005%). They used the ELISA direct screening test, with the ELISA, Western Blot and unspecified other tests as confirmatory tests.
b. In order to discourage high risk donors from donating, a pamphlet was provided to homosexual groups and information from the blood transfusion centre was put into newspapers.
c. In the event that a donor tested positive for HLTV-III, they would be seen by their physician '*with help from BTC's and specialised Centres*'.
d. There were anonymous community testing sites available.

245. An article written in March 1988 published in a Belgian journal suggests that a switch was being made to heat treated products in Belgium in 1986.[346]

246. In a survey of haemophilia conducted by the Council of Europe in around June 1989, the Belgian authorities reported that its association of patients with haemophilia was most concerned about the importance of self-sufficiency in Belgium, opposing the importation of commercial product as far as possible. Seropositivity was at 5% amongst patients with haemophilia.[347]

247. In February 1992, Dr Gunson made enquiries with other countries about their donor leaflets '*to ensure that donors with high risk activities which may give an increased risk of HIV do not donate blood.*'[348] He received a leaflet from Belgium. [349] This leaflet

[344] DHSC0002289_065; DHSC0003893_021.
[345] PRSE0003860.
[346] RLIT0001906.
[347] NHBT0004024_003.
[348] NHBT0007305_001.

stated that a person could not give blood if they were a male homosexual or bisexual, an active prostitute, an AIDS patient, had 'anti-AIDS antibodies', had had sexual contact with any of those groups or had stayed in a country where AIDS was *"endemic (Africa, Caribbean Islands')"*.

Prevalence

248. According to a draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, by 20 October 1983 Belgium had reported 38 cases of AIDS to the WHO. Belgium reported the number of cases under each "Year of Diagnosis" as 1980 (2), 1981 (4), 1982 (8) and 1983 (24).[350]

249. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[351] The following information about the prevalence of HTLV-III in Belgium is set out:

a. As at December 1985, the population of Belgium was 10 million.
b. There had been 139 cases of HTLV-III of which 98 had died.
c. 2 of these had been infected via blood transfusions (excluding people with haemophilia).
d. Of the 850 people with haemophilia A in Belgium, 340 were in receipt of regular treatment. 225 of those with haemophilia A had been tested for HTLV-III. 10 (or 4%) were positive. None had developed AIDs.
e. There were 150 people with haemophilia B. Of those 60 were regularly treated. 45 had been tested for HTLV-III. None were positive.
f. 220 patients who were only treated with cryoprecipitate were tested for HTLV-III. 7 were positive.

250. An article written in March 1988 provides as follows[352]:

[349] NHBT0007305_003 at p.4.
[350] CBLA0001775 at p.35.
[351] PRSE0003860.
[352] RLIT0001906.

a. A countrywide survey by the Red Cross in 1986 of 291 people with haemophilia reported that 19 were confirmed HIV positive. 9 of those (47%) were from one centre which looked after only 10% of the country's people with haemophilia.
b. Since that survey there had been a further 4 cases.
c. The prevalence of HIV in Belgian people with haemophilia in March 1988 was thought to be 6.5% compared to 30 – 90% in almost all Western industrial countries.
d. The authors put this down to a policy of self-sufficiency in blood components initiated 'well before' AIDS came to notice, 'policy during the AIDS epidemic and luck'.
    i. With respect to the policy of self-sufficiency, 90% of Belgian people with haemophilia had never received imported Factor VIII products since well before 1980.
    ii. The element of luck was said to be because HIV appeared later and in lower numbers in Belgium blood donors than in American ones, although it was unclear how much of that was due to the fact that blood donors in Belgium were voluntary and unpaid.
    iii. The policy during the AIDS crises consisted of a policy of self-exclusion of AIDS risk groups from blood donation since 1983, with HIV screening being performed on plasmapheresis donations before it was imposed by law on 1 August 1984

251. The article also notes that there had been 21 HIV infections from blood transfusion *"a figure which ..... puts Belgium in the same range as the United Kingdom and Italy"*.

252. At the time of a survey of haemophilia conducted by the Council of Europe in around June 1989 seropositivity was at 5% amongst patients with haemophilia.[353]

253. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, 4 people with haemophilia and 61 transfusion recipients were reported as having AIDs in Belgium.[354]

[353] NHBT0004024_003.
[354] NHBT0010038_001 at p.25.

254. In a memo (which appears to be from the Belgian authorities to the UK authorities) dated 1990, it is reported that a total of 86 people were infected with AIDS through blood transfusions in Belgium before screening began in 1985.[355]

255. A British Medical Journal article states that between 1985 and 1993, 9 cases of AIDS were identified amongst people with haemophilia in Belgium.[356] The following table within the report shows the breakdown of AIDs cases associated with blood products per million in different patient groups.[357] The article does not specify the blood product associated with these cases.

Year	**Annual incidences of AIDS cases associated with blood/blood products in patients with haemophilia**	**Annual incidences of AIDS cases associated with blood/blood products in transfusion patients**
1985-87	*0.00*	*0.66*
1988-89	*0.23*	*0.98*
1991-93	*0.15*	*0.99*

256. Historic prevalence rates of HIV in Belgium were discussed at the international Congress of the World Federation of Haemophilia, held in Mexico in 1994.[358] It was reported that because Belgium invested in self-sufficiency from voluntary donation in the seventies, it "*largely escaped the HIV scourge*". In 1986, 7% of haemophilia patients were HIV positive and none of Belgium's regular plasma donors were HIV positive.

Denmark

Information about treatment by way of blood and blood products

[355] DHSC0038699_107.
[356] DHSC0004556_067 at p.2, Table 1.
[357] DHSC0004556_067 at p.2, Table 2.
[358] BPLL0016001_001 at p.11.

257. In 1986 Denmark reported to the European Council that it was responsible for the care of 310 people with haemophilia: 250 with haemophilia A and 60 with haemophilia B.[359] Of those with haemophilia A, 130 people were in treatment and 60% of these patients were HTLV III positive.[360]

258. A study by M Melbye[361] referred to in a letter to *The Lancet* of 22 people with haemophilia from Denmark who had been treated with Factor VIII concentrate purchased from US and European commercial sources demonstrated a high prevalence of LAV; 14 of the 22 were positive (64%).[362] It concluded as follows:

> *"In Denmark, cryoprecipitate concentrates[363] may be purchased from the United States or European commercial sources. However, since the cryoprecipitate concentrate commercially manufactured in Europe uses large quantities of sera purchased from the United States, the distinction about place of manufacture is likely to be important only if it is also certain that sera used in the manufacture are obtained solely from populations at low risk of AIDS*
>
> *Clinicians caring for haemophiliacs should consider alternative forms of therapy for the care of new patients not yet exposed to cryoprecipitate concentrates. ..... until screening tests or techniques to neutralise the agent are in widespread use commercially available cryoprecipitate products should be considered as probably contaminated."*

Steps taken in relation to blood donors

259. In a report for the Council of Europe Committee of Experts on Blood Transfusion and Immunohaematology in May 1983, Denmark reported that no measures had been taken by transfusion centres in relation to the selection of blood donors.[364] A group of experts was working on the issue and the current proposal was for an announcement to be made by blood services asking "*in a discreet and tactful way*" that individuals from groups

[359] PRSE0003860 at p.9.
[360] PRSE0003860 at p.9.
[361] For details of the study see paragraph 273 of this presentation.
[362] PRSE0002859.
[363] It is likely that this means factor concentrates.
[364] DHSC0000717 at p.4.

with high prevalence of AIDS abstain from giving blood, and for donors to be questioned about potential symptoms such as weight loss.

260. A series of measures to exclude at-risk donors followed:
    a. In May 1983, the Danish National Board of Health recommended that all homosexual men refrain from donating blood.
    b. That recommendation was made into a formal request of all blood donors in July 1983 and incorporated into the general blood donor information pamphlet provided to donors in September 1983, which recommended that "*sexually active homosexual or bi-sexual males…addicts who take drugs by injections…persons born and raised in Central Africa or Haiti…and sexual partners (both males and females) of the above risk groups*" should refrain from donating.[365]

261. It was confirmed in the European Health Committee report on 'AIDS Developments in Member States, Finland and Australia' (to accompany its main Meeting Report dated 28-31 May 1985),[366] that '*folders*' with information on AIDS and risk groups were prepared in 1983 by the National Health Service, in collaboration with blood banks and the Danish Voluntary Association, and distributed to all active donors. People from risk groups were asked to refrain from giving blood.

262. On 27 August 1985 the NBH wrote a letter to all the Danish blood banks, requiring them to get blood donors to sign a statement declaring that they had read an AIDS information pamphlet and that they did not belong to any of the risk groups set out there.[367]

263. The UK research in December 1985 on the measures taken by various countries indicates that Denmark was planning a widespread public information campaign and discreet contact with at-risk groups. [368] In addition, there was to be a special campaign involving national service men.

Steps taken regarding viral inactivation

[365] RLIT0000456 at pp.179-180; MACK0002633_009.
[366] NHBT0009083_009.
[367] RLIT0000456 at pp.179-180; MACK0002633_009.
[368] DHSC0002289_065; DHSC0003893_021.

264. The Danish Haemophilia Society and physicians working in the field began to push for the use of imported heat-treated factor concentrate towards the end of 1984 as no Danish manufacturer was able to produce heat-treated products.[369]

265. Before they could be sold and distributed in Denmark, heat treated products from abroad had first to be approved and registered in Denmark. In April 1985 the Danish Haemophilia Society asked the National Board of Health to approve heat treated concentrate for children under 4 and all people with haemophilia who did not have detectable HIV antibody.[370]

266. The WHO issued a global recommendation for heat treatment on 26 April 1985. However, throughout 1985 debate continued within Denmark about whether the benefits of heat treatment had been properly proven and the comparative risk of breaching Denmark's self-sufficiency policy and the consequential stunting of the consumption of Danish product.[371]

267. On 10 September 1985 a general requirement was introduced that all Danish and foreign blood products be heat treated, with a 1 October 1985 cut-off for the distribution of non heat-treated product.[372]

HTLV-III testing

268. The European Health Committee produced a Report on 'AIDS Developments in Member States, Finland and Australia' to accompany its main Meeting Report dated 28-31 May 1985.[373] This confirmed that in Denmark:

    a. A committee had been created to consider LAV testing and heat treatment of national Factor VIII products. Informing positive donors of their results '*is a major problem and is one of the reasons for delaying the screening of donors'*
    b. Some preliminary screening had been carried out by a cancer laboratory. After two rounds of testing and confirmatory testing, no samples were positive.

[369] RLIT0000456 at pp.182-185.
[370] RLIT0000456 at p.182.
[371] RLIT0000456 at pp.182-184.
[372] RLIT0000456 at p.188.
[373] NHBT0009083_009.

c. Several clinics around the country offered anonymous screening for LAV/HTLV-III on demand.

269. On 2 September 1985 a story emerged in the press about a man who had been diagnosed with AIDS and given blood on three occasions between 1983 and 1984. The following day, Denmark announced that it would initiate the screening of all donor blood for HIV-virus antibody through Western blot analysis, which was later made mandatory in all hospitals by January 1986.[374]

270. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[375] The information provided by Denmark as to its response to the risk of HLTV-III was as follows:

a. Screening of blood donations began in January 1986. They had screened 556,170,000 donations. 5 had tested positive (0.007%). They used the ELISA direct screening test, with the Western Blot as a confirmatory test.
b. In order to discourage high risk donors from donating, donors were required to sign to state that they did not belong to specified groups.
c. In the event that a donor tested positive for HLTV-III, they would be seen by the director of the blood transfusion centre, and then followed up by a specialist in infectious medicine.
d. There were community testing sites available, but these were not anonymous.

Prevalence

271. In July 1982 there was a report in the BMJ of four cases of AIDS in men in Denmark.[376]

272. According to a draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, by 20 October 1983 Denmark had reported 13 cases of AIDs to the WHO. Denmark reported the number of cases under each "Year of Diagnosis" as 1980 (1), 1981 (2), 1982 (4) and 1983 (6).[377]

[374] RLIT0000456 at pp.188-189.
[375] PRSE0003860.
[376] PRSE0002691.
[377] CBLA0001775 at p.35.

273. In information provided to the Council of Europe Committee of Experts on Blood Transfusion and Immunohaematology in Lisbon in May 1983, Denmark reported that between May 1980 and February 1983 seven cases of AIDS had been recorded and none of those patients had received blood before the onset of the disease.

274. A study by Melbye published on 7 July 1984 of 22 people with haemophilia from Denmark who had been treated with Factor VIII concentrate purchased from US and European commercial sources demonstrated a high prevalence of LAV; 14 of the 22 were positive (64%).[378]

275. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[379] The following information about the prevalence of HTLV-III in Denmark is set out:

a. As at March 1986, the population of Denmark was 80 million.
b. There had been 80 cases of HTLV-III of which 51 had died.
c. One of those had been infected via blood transfusions (excluding people with haemophilia).
d. Of the 250 people with haemophilia A in Denmark, 130 were in receipt of regular treatment. 60% of those were positive for HTLV-III. 3 had developed AIDs.
e. There were 60 people with haemophilia B. 30 of them were in receipt of regular treatment. There was no information as to whether or not they had been tested for HTLV-III.

276. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, 15 people with haemophilia and 12 transfusion recipients were reported as having AIDs in Denmark.[380]

277. In a research paper by Ingvorsen et al. published in 2019, it is stated that between 1975 and 1985 a total of 91 Danish patients with moderate and severe haemophilia were infected with HIV.[381]

[378] PRSE0002859.
[379] PRSE0003860.
[380] NHBT0010038_001 at p.25.
[381] RLIT0000537 at p.1.

Finland

278. Much of the information on Finland comes from the (unsigned) expert report prepared by Dr Juhani Leikola for the Australian HIV litigation in (probably) July 1990,[382] his oral evidence in that case,[383] and his statement made to the Penrose Inquiry.[384] Dr Leikola was the director of laboratory services for the Finnish Red Cross Blood Transfusion Service between 1975 and 1981, head of the blood programme at the League of Red Cross and Red Crescent Societies in Geneva between 1982 and 1986, and then director of the Finnish Red Cross Blood Transfusion Service from February 1988.

Knowledge of risk

279. According to Dr Leikola, by April 1983 there was relatively strong evidence that AIDS was being transmitted through blood products, and there was suspicion that commercial Factor VIII concentrates prepared from large pools of US plasma were the source of the infection.[385]

Response to risk

280. In a document dated 28 April 1983 setting out the information provided for the meeting of Council of Europe's Committee of Experts on Blood Transfusion and Immunohaematology to discuss AIDs, which took place in May 1983, Finland made it clear that they were not at that time taking any measures in response to AIDS, rather they outlined the measures that were under consideration:

> *"... for the time being, it would be impossible to try to identify donors with abnormal sexual preferences. It can only be hoped that the risk will be lower in a voluntary non-remunerated blood transfusion system than in a paid system.*
>
> *Any attempt to improve national self-sufficiency would diminish or eliminate import of possibly infected products from "endemic areas". As the pool size might influence the risk of transmission, it would be advisable to limit the size and give preference to small pool preparation eg, cryoprecipitate.*"[386]

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[382] CBLA0000016_026.
[383] CBLA0000066_004.
[384] PRSE0003241.
[385] CBLA0000016_026 at para 1.
[386] DHSC0000717.

Measures taken regarding donors

281. In November 1983 an article in a Finnish newspaper reported that there was as yet no official recommendation in Finland advising high risk groups to refrain from donating, but a leaflet was being developed recommending that those in high risk groups should not donate blood.[387]

282. The first information leaflet given to donors was in February 1985. This advised homosexual men not to give blood.[388] The information given by Finland to the Committee of Experts on Blood Transfusion and Immunohaematology for their conference in May 1986 confirmed that in order to prevent high risk donors from donating, Finland provided donors with a leaflet prior to donating.[389]

283. In Professor Leikola's oral evidence in the *PQ v Australian Red Cross Society* litigation, he stated that strong connections between donation services and the Association of Sexual Minorities meant that the message to homosexual males not to donate worked well as a first self-exclusion screen for blood donation.[390]

284. From October 1985 the donor was required to sign a health statement.[391]

285. In February 1992, Dr Gunson made enquiries with other countries about their donor leaflets '*to ensure that donors with high risk activities which may give an increased risk of HIV do not donate blood.*'[392] He received a sample leaflet from Finland.[393] This stated that the following persons must not give blood or plasma:
    - *people, who suspect of having HIV infection (sic)*
    - *people, who have been shown to have HIV antibodies, and their sexual partners*
    - *men, who have had sex with other men, and their female sex partners*
    - *drug abusers, ie people, who are using or have ever used intravenous drugs, and their sex partners*

[387] PRSE0003241 at para 4.
[388] PRSE0003241 at para 6; CBLA0000066_004 at p.35.
[389] PRSE0003860.
[390] CBLA0000066_004 at pp.34 - 35.
[391] CBLA0000066_004 at p.35.
[392] NHBT0007305_001.
[393] NHBT0007305_003 at p.6.

- *people, who have been living in areas where HIV is common in the population (eg certain metropolitan areas in the USA, some Central American countries and countries in Equatorial Africa), and their sex partners*

Screening of blood donations

286. During early summer of 1985 there was a pilot study to look at HTLV-III screening of blood donations.[394] This was performed on 10,000 Helsinki donations.[395] One donor was found to be positive.

287. Thereafter:
    a. Screening of all donors in the Helsinki area began on 1 September 1985.
    b. Donations from other centres and mobile sessions began to be screened by 1 January 1986 (i.e. all other donations).[396]
    c. All blood donations were tested by the Finnish Red Cross.[397]
    d. They used the ELISA direct test with the Western Blot test as a confirmatory test.[398]
    e. In the event that a donor tested positive for HTLV-III, they would see a physician at the Blood Transfusion Centre, and then be followed up by an appropriate specialist.[399]
    f. There were anonymous community testing sites available from September 1985.[400]

Measures taken regarding blood products

288. The Finnish Red Cross Blood Transfusion Service did not include a warning on the possible risk of AIDS or HIV transmission in the label or in the information insert of its cryoprecipitate.[401]

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[394] PRSE0003241 at para 6.
[395] CBLA0000066_004 at p.41.
[396] PRSE0003241 at para 6.
[397] DHSC0002289_065.
[398] PRSE0003860.
[399] PRSE0003860.
[400] PRSE0003241 at para 7.
[401] CBLA0000016_026 at p.5.

289. In either December 1984 or January 1985, the Finnish Red Cross Blood Transfusion Service began to heat treat its Factor VIII concentrate.[402] The method was available on a larger scale in May 1985. Clinical trials were performed in July/August 1985. All concentrate was heat treated by October 1985.[403] There was however no recall of product, and so those on home treatment continued to use unheated product until August 1985.[404]

290. In 1987 steps were taken to treat cryoprecipitate to inactivate HTLV-III.[405]

Prevalence

291. In Professor Leikola's oral evidence to *PQ v Australian Red Cross Society,* he suggested:
    a. That the geographic isolation, cold weather and lifestyle/culture of Finland meant that it was not an attractive place for people in high-risk groups to visit, which left the donor population almost completely infection-free.[406]
    b. That in the autumn of 1984 there were four HIV positive donors in Finland. Of the recipients of blood products from those donors, four tested HIV positive. A further two donors were found to be HIV positive in 1985 and the patient to whom they donated platelets developed symptoms of a new HIV infection but died of her severe underlying disease soon after.[407]

292. According to a draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, by 20 October 1983 Finland had reported 2 cases of AIDs to the WHO in 1983 (the "Year of Diagnosis").[408]

293. From the beginning of 1986 there were no new HIV transmissions through blood products in Finland.[409]

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[402] PRSE0003241 at para 13.
[403] CBLA0000066_004 at p.42.
[404] PRSE0003241 at para 13.
[405] CBLA0000066_004 at p.67.
[406] CBLA0000066_004 at p.32.
[407] PRSE0003241 at para 18.
[408] CBLA0001775 at p.35.
[409] DHSC0002937_012.

294. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, set out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[410] The following information about the prevalence of HTLV-III and AIDS in Finland was provided:

a. As at March 1986 the population of Finland was 4.8 million. There had been 11 cases of HTLV-III. Six had died.

b. There were 250 people with haemophilia A in Finland. Of them, 180 received regular treatment. 150 had been tested. 2 had tested positive (or 1.3%). Neither had developed either AIDS or AIDS regional complex. They were both infected by cryoprecipitate, one was infected in 1983 and before the beginning of 1985.[411]

c. There were 40 haemophilia B patients in Finland. Of them, 20 were in receipt of regular treatment and all of them had been tested. None of them were HTLV-III positive.

295. Finland completed the Council of Europe Committee of Experts on Blood Transfusion and Immunohaemotology questionnaire in 1987. It reported that 666,000 donations from 200,000 donors had been tested for anti-HIV up to the end of December 1987. Five confirmed positives were found up to the end of December 1987 and one in February 1988.[412]

296. The 1987 questionnaire included information on a look back exercise concerning donations going back to 1 January 1982. 32 patients were known to have received products since 1 January 1982 from infected donors. 8 were anti-HIV negative. 3 were not traced. 6 were anti-HIV positive, of whom two died of AIDS.

297. A study was conducted on 6 severe haemophilia patients receiving home therapy delivered Finnish dry-heated concentrate between 1985 and 1991. The batches used in that time came from a total of 3,000 donor plasmas and there were 1.1 million units used by the six patients across that period. None of the patients were anti-HIV positive.[413]

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[410] PRSE0003860.
[411] PRSE0003241 at para 16. See also RLIT0000469.
[412] NHBT0004514_009 at pp. 2-3.
[413] MACK0000787_047.

298. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, that no person with haemophilia and three transfusion recipients were reported as having AIDs in Finland.[414] This data is at odds with that set out above.

299. In September 1995, the UK received information on HIV and HCV from Dr Leikola. He stated that there were 2 HIV positive people with haemophilia and 6 HIV positive blood recipients in Finland. The population of Finland was 5 million (compared to 56 million in the UK). He was of the view that the reason for the low incidence of HIV in Finnish people with haemophilia was because prior to 1985:

(i) Most patients were given cryoprecipitate which involved smaller pools and fewer overall donations to each patient.

(ii) Finland did not import from the US or use Factor VIII concentrate from paid donors.[415]

Norway

Selection of donors

300. In information provided to the Council of Europe, Committee of Experts on Blood Transfusion and Immunohaematology for their meeting on 16-19 May 1983, Norway stated that the Health Authorities were preparing recommendations to the blood transfusion centres for selection of donors and preparing information materials to be '*spread among blood donors'*.[416] However in the Blood Bank of Ulleval Hospital, measures had already been introduced for the selection of donors, requiring them to sign a questionnaire which included the following text:

"NB: A life-threatening defect of the defence mechanism of the body against infections and certain tumors which may be transmitted also by blood transfusion has been detected in some male homo/heterosexuals, especially in those having various and scattered sexual contacts. No effective treatment of the condition is known, and it

[414] NHBT0010038_001 at p.25.
[415] DHSC0003552_045.
[416] DHSC0000717.

has a high mortality rate. The carrier state cannot be demonstrated by laboratory tests, and the incubation period may be very long.

So long as the situation has not been made clear we hereby earnestly ask male homosexuals and persons with numerous sexual contacts not to donate blood.

The physicians of the blood bank are at your disposal if you want further information."

301. Norway's suggestion to the Committee was that similar measures to this should be introduced at European level, with a specially designed follow-up form being sent to the reporting physician.

302. The European Health Committee produced a Report on AIDS Developments in Member States, Finland and Australia, to accompany its main Meeting Report dated 28-31 May 1985.[417] It reported that in Norway an advisory group on AIDS had been organised by the Norwegian Health Authorities. Following a recommendation from this group, the health authorities had asked all blood banks to inform all donors about AIDS.

303. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[418] Norway stated that in order to discourage high risk donors from donating, a leaflet was provided to donors, before donating, and they were asked to sign a statement.

304. In February 1992, Dr Gunson made enquiries with Western Europe about their donor leaflets '*to ensure that donors with high risk activities which may give an increased risk of HIV do not donate blood.*'[419] He received a letter from Norway setting out what was in the 1991 version of the donor leaflet.[420] It was a leaflet that all donors had to read and sign. The risk groups were described as:

- *Men who have had sexual contact with men*

[417] NHBT0009083_009.
[418] PRSE0003860.
[419] NHBT0007305_001.
[420] NHBT0007305_003 at p.14.

- *Persons who have abused narcotics*
- *Persons who have had sexual contact with patients suffering from AIDS or hepatitis, or with persons who have had a positive test for one of these diseases.*
- *Prostitutes/former prostitutes*
- *Persons who during the last 5 years have had sexual contact with prostitutes*
- *Persons who during the last 6 months have had one or more casual or unknown sexual partners*
- *Persons who have received blood transfusions outside Europe*
- *Persons who during the last 5 years have had sexual contact with persons belonging to the above mentioned risk groups.*

Testing of donations

305. Norway informed the European Health Committee for its report on AIDS Developments in Member States, Finland and Australia, in May 1985 about the steps taken in relation to the testing of donations:
    a. Persons belonging to any risk groups were asked to refrain from blood donations.
    b. Screening of blood donors for the presence of LAV/HTLV-III antibodies had started recently at a few larger centres. They had been screened anonymously as part of a pilot project.
    c. Before universal screening was to be introduced, a parallel service (outside the transfusion service) needed to be set up. A clinical counselling service for persons found to have LAV/HTLV-III antibodies would also need to be available.
    d. '*A major proportion'* of Norwegian people with haemophilia had been tested for the presence of anti-LAV/HTLV-III. Antibodies were found in 12% of the patients, but no confirmatory tests were available. [421]

306. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out

[421] NHBT0009083_009.
[422] PRSE0003860.

by Dr Gunson.[422] The information provided by Norway as to its response to the risk of HLTV-III is as follows:

a. Screening of blood donations began in April 1985. They had screened 150,000 donations. 2 had tested positive (0.001%).
b. They used the ELISA direct screening test, with the Western Blot and unspecified other tests as confirmatory tests.
c. In the event that a donor tested positive for HLTV-III, they would be seen by a physician at the blood transfusion centre, and then referred to a specialist in infectious diseases.
d. Those patients who had received blood from antibody positive donors were followed up.
e. There were anonymous community testing sites available.

Viral inactivation

307. In 1985 the Norwegian Health Authorities decided that plasma, cryoprecipitate and Factor IX should be replaced by virus inactivated plasma products prepared from Norwegian plasma by 1988.[423] This target appears to have been met.[424] Since 1988, virus inactivation by SD treatment had been the standard procedure for plasma products with dry-heat treatment or nanofiltration being used for coagulation factors.

308. In 1986, a pilot project for contract fractionation was initiated by the Red Cross and National Hospital Blood Centre.[425] Throughout 1987-1988 an increasing number of blood banks joined. The project collected plasma from all the blood banks in the country and contracted for its fractionation and/or viral inactivation on the European market. The project then returned the fractionated products to the blood banks.[426] This initiative is said to have contributed to virally inactivated plasma products with the retention of self-sufficiency.[427]

Miscellaneous measures

[422] PRSE0003860.
[423] RLIT0001244 at p.2.
[424] RLIT0001245 at p.3.
[425] RLIT0001244 at p.2.
[426] RLIT0001244 at p.2.
[427] RLIT0001244 at p.2.

309. The UK did some research on the measures taken by various countries, probably in December 1985[428] (the table setting out the research is undated but there is a letter circulating it dated 17 December 1985).[429] In so far as Norway was concerned:

a. They had plans 'in the near future' to amend legislation to encompass AIDS to introduce measures similar to the UK.
b. An expert group had been appointed to conduct research into the national and international situation and to consider the care of sufferers.
c. There was a programme for the screening of blood donors.
d. Principles had been drawn up to prevent the spread of the disease and practical measures had been outlined that could be taken.

Prevalence

310. It is estimated that there was a prevalence of anti-HIV of 6% in the whole Norwegian haemophilia population in the early 1980s.[430]

311. According to a draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, by 20 October 1983 Norway had reported 2 cases of AIDs, both diagnosed in 1983.[431]

312. By the spring of 1985, some Norwegian people with haemophilia had developed antibodies to HIV, and the use of American concentrates was initially blamed.[432] It later appeared that several HIV positive Norwegian people with haemophilia had been infected through the use of cryoprecipitate prepared in national blood banks.[433] During 1985-1986, 334 of 389 (86%) registered Norwegians with coagulation factor defects were screened for HIV antibodies, and 21 were confirmed as HIV positive.[434] These were all patients with clinically severe haemophilia A and represented 18.4% of 114

[428] DHSC0002289_065.
[429] DHSC0003893_021.
[430] RLIT0001244 at p.2.
[431] CBLA0001775 at p.35.
[432] RLIT0001245 at p.5.
[433] RLIT0001245 at p.5.
[434] RLIT0001245 at p.1.

tested persons with severe haemophilia A.[435] At least 8 of the 21 cases were infected through lyophilised cryoprecipitate prepared from volunteer plasma donated in national blood banks.[436] The report's authors considered it likely but not proven that another 3 of the 21 were infected in the same way.[437]

313. It was reported that the evidence suggested that 2 of the 8 seroconversions mentioned above were not treated with American concentrate but received cryoprecipitate from HIV positive Norwegian blood donors in 1983/1984.[438] The other 6 of the 8 were found anti-HIV positive without ever having received commercial concentrates.[439] The 3 people with haemophilia treated with American concentrates in 1980/1981, all remained seronegative for 1-2 years before receiving cryoprecipitate from documented anti-HIV positive Norwegian blood donors, and then seroconverted.[440] It was considered unlikely that the HIV infections came from the cryoprecipitate imported from the Finnish Red Cross, as only 3% of persons with severe haemophilia in Finland had HIV antibodies.[441]

314. In a journal article entitled 'HIV infection in Norwegian haemophiliacs: The prevalence of antibodies against HIV in haemophiliacs treated with lyophilized cryoprecipitate from volunteer donors' by SA Evensen and others published in Eur J Haematol in 1987 in which this study was reported, the authors concluded *"that the prevalence of HIV antibodies among haemophiliacs in Norway is among the lowest in Western Europe. To our knowledge, only Finland ranks lower"*.

315. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[442] The following information about the prevalence of HTLV-III in Norway is set out:

    a. As at March 1986, the population of Norway was 4 million.

[435] RLIT0001245 at p.1.
[436] RLIT0001245 at p.1.
[437] RLIT0001245 at p.5.
[438] RLIT0001245 at p.5.
[439] RLIT0001245 at p.5.
[440] RLIT0001245 at p.5.
[441] RLIT0001245 at p.5.
[442] PRSE0003860.

b. There had been 21 cases of HTLV-III of whom 15 had died.
c. 1 of those had been infected via blood transfusions (excluding people with haemophilia).
d. Of the 225 people with haemophilia A in Norway, 140 were in receipt of regular treatment. 225 of those with haemophilia A had been tested for HTLV-III. 19 (or 8%) were positive. One had developed AIDs and one had developed AIDS Regional Complex.
e. There were 80 people with haemophilia B, of whom 20 were in receipt of regular treatment. All 80 had been tested for HTLV-III. None were positive.

316. In a December 1987 survey of anti-HIV tests on blood donations, Norway tested 500,437 donors and only 2 (0.0004%) were confirmed as positive.[443]

317. By 1988:
f. No haemophilia B patients were anti-HIV positive;
g. Six patients who had received transfusions had been infected with HIV and three had developed AIDS.[444]

318. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, 7 people with haemophilia and 11 transfusion recipients were reported as having AIDS in Norway.[445]

Iceland

319. The European Health Committee produced a Report on 'AIDS Developments in Member States, Finland and Australia', to accompany its main Meeting Report dated 28 to 31 May 1985. [446] It reported that in Iceland, screening for LAV/HTLV-III was due to start in September 1985, with screening being made available to individuals in the risk

[443] NHBT0004514_001 at p.3.
[444] NHBT0004515_002 at p.4.
[445] NHBT0010038_001 at p.25.
[446] NHBT0009083_009.

groups at the same time. No decision had been made about whether to tell donors who were found to be positive.

320. Information gathered on the international situation with AIDS by the UK authorities in December 1985 indicated that recommendations had been made to Ministers in Iceland that AIDS be treated as a sexually transmitted disease (which would involve amending the law).[447] Ministers were also considering adding it to the list of infectious diseases, to allow wide powers of quarantine and other restrictive measures to be put in place. The document is silent on the question of the commencement of donor screening.

321. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[448] This noted the following in respect of the response to risk in Iceland:

a. Notices warning high risk groups not to donate were put up at blood collections sessions. For those donors found to be positive for HTLV-III, the follow up arrangement was for an appointment with a consultant with an immunologist.
b. HTLV-III screening commenced between May and November 1985. 63,000 donations had been screened, of which 2 had been identified as positive (0.003%). Iceland used the Competitive ELISA test and the Western Blot as a confirmatory test.
c. There were alternative testing sites in the community that tested those who attended, anonymously.

322. Iceland filled out a questionnaire for a Council of Europe meeting held between 3 and 6 May 1988. The questionnaire was dated 31 March 1988.[449] It reported that testing for anti-HIV was performed on every blood donation using the direct ELISA test, with the Western blot as the confirmatory test. There had been no positive results found up to the end of December 1987. Information on AIDS to discourage high risk donors from donating was provided to all Icelandic donors by way of guidelines before each

[447] DHSC0002289_065 at p.3 .
[448] PRSE0003860.
[449] NHBT0004514_017.

donation, and anonymous anti-HIV testing for non-blood donors was available at alternative sites. It was noted that Factor VIII had been imported from Finland over the past 12 years.

323. There was a Council of Europe survey of haemophilia which is undated, but from other correspondence is probably around June 1989. [450] Iceland reported that Factor VIII had been imported, principally from Finland, until 1988, and cryoprecipitate had been used. No people with haemophilia had been HIV infected and no legal proceedings had been instituted.[451]

324. In February 1992, Dr Gunson made enquiries with Western Europe about their donor leaflets '*to ensure that donors with high risk activities which may give an increased risk of HIV do not donate blood.*'[452] He received a form from Iceland.[453] This asked the following people to refrain from donating blood:

a. Those infected with HIV.
b. Those who are homosexual and bisexual.
c. Those who are promiscuous or have had sex with a prostitute.
d. Those who have been drug abusers in the past or use drugs at present.
e. Those who have lived in Haiti or Central Africa.
f. Those who have been treated with acupuncture by non-medical practitioners, had tattooing, or ears pierced during recent years.
g. Those who have had sexual contact with any person in the above category.

Prevalence

325. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[454] This noted the following in respect to prevalence in Iceland:

[450] NHBT0004024_002.
[451] NHBT0004024_003 at p.3 (under cover of letter NHBT0004024_003).
[452] NHBT0007305_001.
[453] DHSC0020707_045.
[454] PRSE0003860.

a. As at May 1986, Iceland had a population of 0.24 million. They had 2 cases of HIV and one death. Both those cases were homosexuals.
b. In terms of infection, of those with haemophilia, there were 10 patients with haemophilia A, all of whom received regular treatment. They had all been tested and none of them were positive. There were 2 patients with haemophilia B who were rarely treated. They had not been tested.

326. Iceland filled out a questionnaire for a Council of Europe meeting held between 3 and 6 May 1988 (with the questionnaire being dated 31 March 1988). [455] It revealed that look backs had been carried out. These had identified one HIV woman who tested positive for HIV in 1986 having received infected blood in 1983. It also stated that repeated testing of all people with haemophilia in Iceland had revealed that they were all negative.

327. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, no person with haemophilia and 2 transfusion recipients were reported as having AIDS in Iceland.[456]

328. UK surveillance data indicates that as of 19 November 1990 Iceland had 14 cases of AIDS in the entire population.[457]

Spain

329. Information provided to the Committee of Experts on Blood Transfusion and Immunohaematology for their May 1983 meeting proposed *"a very strict control in the selection of the donors of plasma for the obtainment of hemoderivatives (principally coagulation factors)"* at European level, despite not having put any measures in place themselves. [458]

[455] NHBT0004514_017.
[456] NHBT0010038_001 at p.25. See also NHBT0019285_006.
[457] NHBT0008408_038.
[458] DHSC0000717.

330. The European Health Committee produced a Report on AIDS Developments in Member States, Finland and Australia, for its meeting in August 1985 which reported that (in May 1985):

a. A committee on AIDS had been set up by the Ministry of Health. It was planning a study to find out the positivity rate of LAV/HTLV-III antibodies among the donor population. 10 blood banks were to be involved in the study which was due to start after the summer.
b. No decision had been made as to whether or not to tell donors about a positive result. [459]

331. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson .[460] This noted the following in respect to the response from Spain:

a. Leaflets and brochures were given to donors about AIDS.
b. Spain was the only country in which screening of all blood donations was not mandatory (although it took place in some regions and 14,523 donations had been tested and 0.06 had been found to be positive).
c. There were no arrangements for counselling of positive donors.
d. There were no community testing sites.

Prevalence

332. In April 1983 Spain detected three AIDS patients with haemophilia (one of whom had already died), all of whom had been treated with commercial concentrate[461] sourced from the USA.[462]

333. According to a draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, by 20 October 1983 Spain had reported 6 cases of AIDs to the WHO. Spain reported the number of cases under each "Year of Diagnosis" as 1981 (1),

[459] NHBT0009083_009.
[460] PRSE0003860.
[461] DHSC0000717; PRSE0002321.
[462] CBLA0000043_040.

1982 (1) and 1983 (4).[463]

334. As of 25 September 1984, Spain's population of people with haemophilia had two individuals with AIDS, 58 with AIDS Related Complex (ARC) and one AIDS related death.[464]

335. The number of AIDS cases identified by May 1985 in Spain was 14, with three people with haemophilia infected and three cases caused by blood transfusion.[465]

336. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[466] This noted the following in respect to the prevalence in Spain:

a. As at December 1985, Spain had a population of 46 million.
b. It had had 83 cases of AIDS and 59 deaths. Of those, none had been a recipient of a blood transfusion.
c. Of the 2005 people with haemophilia A in Spain, 68% had tested positive for HTLV-III and 25 had AIDS.
d. There were 320 people with haemophilia B. No details were given as to how many of these people were tested for HTLV-III, but one had developed AIDS.

337. Figures obtained by the World Haemophilia AIDS Centre in June 1987 from one Spanish haemophilia centre with 315 patients, provided that of the 148 people there with severe haemophilia A, 124 were HIV positive (84%), out of 64 patients with moderate haemophilia A, 64 of them were HIV positive (72%), and for those 54 with mild haemophilia A, 13 had HIV (24%).With respect to those with haemophilia B – out of the 23 people with the severe form, 17 of them were HIV positive (74%), out of the 19 with the moderate form, 6 of them

[463] CBLA0001775 at p.35.
[464] BAYP0000024_068 at p.2.
[465] NHBT0009083_009 at p.9.
[466] PRSE0003860.

were HIV positive (32%), and out of the seven people with mild haemophilia B, 4 of them were positive (52%). There had been 7 AIDS cases by June 1987.[467]

338. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, 263 people with haemophilia and 93 transfusion recipients were reported as having AIDs in Spain.[468]

Italy

Knowledge of risk

339. In 1982 the first cases of pneumocystis carinii pneumonia and Kaposi's sarcoma were reported in Italy. The first AIDS case was reported in 1984.[469]

340. In May 1983 the Instituto Superiore di Sanita[470] (ISS) published an article in its newsletter, reporting American data on AIDS in patients with haemophilia and highlighting the causal link between AIDS and the use of commercial American factor concentrate from large donor pools.[471]

341. At the beginning of 1984, an Italian research group led by Mannucci published 'Abnormalities of Lymphocyte subset are correlated with concentrate consumption in asymptomatic Italian people with haemophilia treated with concentrates made from American plasma' in the American Journal of Haematology.[472] This set out their findings that out of 83 symptom free people with haemophilia who had been treated with American factor products, 4% had lymphopenia, 49% had decreased T-helper/T-suppressor cell ratios and 2% had both. The paper concluded:

"The most important finding in our study was the clear cut association between abnormalities of the T-lymphocyte subpopulations and the amount of concentrate used in the year preceding the blood testing. In haemophiliacs treated with less than 20,000 U/yr, abnormalities were generally no more

[467] BART0000619 at p.5.
[468] NHBT0010038_001 at p.25.
[469] RLIT0000456 at p.233.
[470] The National centre for research, control and technical-scientific advice on public health in Italy.
[471] RLIT0000456 at p.233.
[472] BAYP0000026_015.

frequent and pronounced that in healthy controls or untreated haemophiliacs, whereas abnormalities were much more frequent and pronounced in haemophiliacs treated with annual dosages greater than 20,000 U.

……..

Abnormal lymphocyte subpopulations per se cannot yet be used for diagnostic evidence of AIDS or its prodrome; only by longitudinal studies of asymptomatic haemophiliacs with abnormal values can the relevance of such tests to AIDS risk be established. Therefore, we cannot recommend using less than 20,000 U/yr in an attempt to prevent AIDS solely on the basis of these data. We continue our present policy of giving to the patients all the factor they need, on demand, for treatment of haemorrhages and elective surgery. However, we avoid long-term prophylaxis in an attempt to prevent all haemorrhage because there is not proof that such prophylaxis results in better prevention of haemophiliac arthropathy, while it does result in much larger concentrate consumption."

342. In March 1985, members of the Italian Haemophilia Foundation received a therapeutic handbook edited by the Scientific Committee of the Foundation (Pier Mannucci being its director) which stated that:

"Only one haemophiliac in 1,000/2,000 has full-blown AIDS in the USA and other European countries; on the other hand, cases among non-haemophiliacs in Italy amount to no more than 20/30, as compared with 200/300 in other European countries similar in size to Italy, like England, France and Germany. It would seem, then, that the Italian haemophiliac has greater defensive powers, and it is to be hoped that this tendency will be confirmed!"[473]

343. A draft of a report Manucci was asked to provide for the HIV litigation can be found at BPLL0001352.

Treatment policies

[473] As quoted in RLIT0000456 at p.234

344. The Italian Haemophilia Foundation therapeutic handbook (1985) advised that the first results obtained using dry-heat or pressure methods to inactivate the AIDS virus were very encouraging. [474] It concluded that on the basis of that data the Foundation could give a set of important messages to the Italian people with haemophilia:

"AIDS has not appeared in Italy; the risk of new concentrates is lower than old ones, or may even by nil. Therefore there is no reason to abandon, reduce or, at any rate, change the treatment programs and the concentrate dosages that have proved able to transform the haemophiliac state from a state of dependence and permanent frustration to a condition of autonomy and free expression of individual capacity."

Donor selection

345. In the information given by Italy to the Committee of Experts on Blood Transfusion and Immunohaematology for their meeting in May 1983 Italy said as follows:[475]

"No special measures have been introduced by transfusions centres for the selection of the donors.

So far, AIDS is too rare a disease in Europe to justify, in our opinion, the introduction of special measures for donor selection."

346. It was reported in the European Health Committee report on 'AIDS Developments in Member States, Finland and Australia', in May 1985 that blood transfusion centres in Italy had been asked to advise donors not to give blood if they were in risk categories. [476]

347. On 17 July 1985 the Health Ministry issued a ministerial circular recommending that at-risk groups should not be allowed to donate blood. The circular was never published in the legal bulletin and so was never legally binding.[477]

[474] As quoted in RLIT0000456 at p.235
[475] DHSC0000717.
[476] NHBT0009083_009.
[477] RLIT0000456 at p.235.

348. On 15 January 1988 the Minister of Health issued a Decree (No 14) which obliged the blood transfusion centres to ask those from at risk categories not to donate.[478] The risk categories were defined as:

a. Anyone who had taken intravenous drugs since 1978.
b. Male homosexuals.
c. Sexual partners of HIV positive individuals.
d. Anyone who had had multiple transfusions since 1978 onwards.
e. The sexual partners of anyone in the above categories.

349. In February 1992, Dr Gunson made enquiries with Western Europe about their donor leaflets.[479] He received a copy of the letter from Italy provided to donors.[480] This stated:

"Some severe infectious diseases, as viral hepatitis, AIDS, syphilis, can be transmitted through blood donations by possible carriers.

Homosexuals, individuals having sex with prostitutes (in the past 6 months) or with intravenous drug addicts, drug addicts themselves are potential risk subjects in this field.

If you have had a similar behaviour we ask you to give up blood donation. You can go away without any explanation or, if you prefer, you can point out to medical doctor that you blood can only be used for laboratory purposes. (sic)"

350. The donor was required to sign this letter.

Screening

351. The Italian Haemophilia Foundation therapeutic handbook (1985) advised that people with haemophilia would be able to screen their serum for LAV/HTLV III using commercial kits available for home use in a few months' time and already available in some centres. However the handbook stated "*It must be recognised…it is still not clear whether the presence of antibodies, detected in about half of the haemophiliac treated with more than 20,000 IU in our Center, signals the actual presence of the virus in the blood or whether it is rather a*

[478] RLIT0001967.
[479] NHBT0007305_001.
[480] NHBT0007305_003 pp.11-12.

sign of remote contact or, maybe, protection…"[481]

352. The use of the Abbot test for HIV was authorised by the Italian Health Ministry in April 1985. The Haemophilia Foundation held a press conference in May 1985 announcing the wholesale availability of the ELISA test and publicly announcing advice that people with haemophilia use only dry heat-treated concentrate.[482]

353. On 17 July 1985 the Health Ministry issued a ministerial circular recommending the introduction of basic precautions against HIV contamination of blood and blood products by testing of blood donors to detect antibodies and recommended the test be introduced as soon as possible. The circular was never legally binding.[483]

354. Some individual regions of Italy acted more quickly in response to the July 1985 Health Ministry recommendation. For example, Lombardy banned the distribution and use of untreated concentrate on 31 July 1985 and enacted mandatory HIV blood testing in November 1985.[484]

355. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[485] The information provided about Italy's response to risk is as follows:

a. Italy started screening blood donations between April and June 1985.
b. They used the Direct and Competitive ELISA test, and the Western Blot as a confirmatory test.
c. Where a donor tested positive, they were invited for follow up at a reference centre.
d. They discouraged high risk donors from donating by the use of posters and leaflets at blood transfusion centres.
e. There were alternative sites for people to be tested, anonymously.

[481] RLIT0000456 at pp.234-235.
[482] RLIT0000456 at p.235.
[483] RLIT0000456 at p.235.
[484] RLIT0000456.
[485] PRSE0003860.

356. In the 1988 European Health Committee's Committee of Experts on Blood Transfusion and Immunohematology questionnaire on AIDS in relation to blood transfusion, Italy reported that testing for anti-HIV was performed on every blood donation. By the end of 1987, 2,720,000 donations had been tested and 381 were confirmed as positive using direct ELISA test and Western blot.[486] Tests for HIV antigen and anti-HIV2 were not being performed but it was hoped that anti-HIV2 would be introduced in 1989 or 1990.

357. On 15 January 1988 the Minister of Health issued a Decree (No 14) which obliged the pharmaceutical companies licensed to produce blood products, or who imported such products, to prepare the products exclusively from blood or plasma that had tested negative for HIV. [487]

Viral inactivation

358. The first decree authorising the marketing of dry-heated Factor VIII concentrate appeared in December 1984.[488]

359. Recommendations for the use of only heat-treated products were made in Italy in January 1985. It is however unclear when patients actually received such product.[489]

360. The wholesale withdrawal of non-heat treated stocks of concentrates from hospitals did not happen until the end of May 1988. [490]

Prevalence

361. In 1982 the collection of data on AIDS cases began, and in June 1984 it was formalised into a National Surveillance system.[491]

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[486] NHBT0004514_019.
[487] RLIT0001967.
[488] RLIT0000456 at p.234.
[489] BPLL0001352 at pp.9-10.
[490] RLIT0000456 at p.236.
[491] RLIT0001960.

362. In November 1986, AIDS was added to the list of diseases subject to compulsory reporting.[492] The obligation came into force in around February 1987.

363. The AIDS Operations Centre (COA) of the ISS was established by decree of the Ministry of Health in January 1987.

364. The information given to the Council of Europe for their meeting in May 1983, on prevalence in Italy stated that there had been one case in Italy since 1981.[493]

365. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[494] The following information on prevalence in Italy was reported:

a. As at March 1986, Italy had a population of 57 million.
b. There had been 190 cases of HTLV-III of whom 80 had died.
c. Four of those cases had been infected via blood transfusion (excluding people with haemophilia).
d. Of the 1,821 people with haemophilia A, 1,395 received regular treatment. 100% of them had been tested and either 48% or 17% had tested positive (both figures are given). Four of them had developed AIDS.
e. Of the 364 people with haemophilia B, 264 of them received regular treatment. They had all been tested and 48% were positive. One of them had AIDS.

366. As of December 31, 1987, 1,478 cases had been notified, of which four were children with haemophilia and five were transfused children.[495]

[492] RLIT0001919.
[493] DHSC0000717.
[494] PRSE0003860.
[495] RLIT0001918.

367. In the 1988 European Health Committee's Committee of Experts on Blood Transfusion and Immunohematology questionnaire on AIDS in relation to blood transfusion, Italy reported [496] that there had been 18 cases of AIDS associated with blood transfusion and 41 cases among people with haemophilia.

368. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, the cumulative cases of AIDS in Italy amounted to 111 people with haemophilia and 115 transfusion recipients.[497]

369. In a 1990 a national survey of patients with bleeding disorders was undertaken by the Instituto Superiore di Sanita. Of 2,839 patients with haemophilia tested for HIV, 26.75% of those with haemophilia A and 47% of those with haemophilia B were found to be infected with HIV.[498] At some unknown date, a table was published which stated that 2,792 people with haemophilia had been surveyed, of whom 47 (2%) had AIDS and 637 (22.8%) had HIV.[499]

370. The numbers infected by HIV in Italy, and the proportion infected by blood, can be seen at RLIT0001959.

371. It can be seen from the figures set out above, that there is a wide variation, dependent on the source. Some of these figures therefore might need to be treated with caution.

France

Knowledge of risk and treatment policies

372. The matters set out below, are very much a summary of some of the key events. The Krever report[500] and the criminal proceedings brought against

[496] NHBT0004514_019.
[497] NHBT0010038_001 at p.25.
[498] RLIT0000456 at p.236.
[499] RLIT0000456 at p.237.
[500] KREV0000001 at pp.815 - 845.
[501] RLIT0001907.

members of the blood transfusion service and the government[501] provide a more in-depth account of the chronology.

373. The first French case of opportunistic infection was seen in a male homosexual in August 1981. By March 1983, 39 cases had been reported.[502]

374. On 18 November 1982, Professor Soulier, then director of the Centre National de Transfusion Sanguine – the National Blood Transfusion Centre (CNTS), wrote an open letter to the Association Francaise des Hemophiles warning them about American blood products. [503]

375. At the start of 1983, only 60 people with haemophilia in France were receiving prophylactic treatment with Factor VIII concentrate.[504] The trend however was for increasing use of factor concentrates and a move away from cryoprecipitate. Distribution in 1983 was expected to be 75% factor concentrates and only 25% cryoprecipitate.[505]

376. Montagnier (French) and Barre-Sinoussi isolated the virus in May 1983[506] and over the next year a blood test for the antibody to the virus was devised by Dr Rouzioux and his colleagues.

377. On 24 March 1983, the Assistant Director of the French Laboratoire National de la Sante (LNS) addressed the Commission Consultative de Transfusion Sanguine (CNTS) on the subject of AIDS and blood. In May 1983 he informed Professor Roux, the director general of health and Dr Netter, the director of the LNS of the risk to people with haemophilia.[507]

378. On 10 May 1983 Travenol informed CNTS that its factor concentrates would soon be heat treated and it offered to send some to CNTS. This offer was declined.[508]

[501] RLIT0001907.
[502] KREV0000001 at p.819.
[503] KREV0000001 at p.837.
[504] RLIT0000456 at p.118.
[505] KREV0000001 at p.837.
[506] KREV0000001 at p.309.
[507] KREV0000001 at p.821.
[508] KREV0000001 at p.827.

379. In June 1983 the AIDS virus (known in France as lymphadenopathy-associated virus or LAV) was found in two people with haemophilia, and there were six suspected cases of LAV in French people with haemophilia, three of whom had been treated with domestic factor concentrates.[509]

380. In July 1983, a French person with haemophilia died of AIDS; this was the first fatal case of AIDS in a person with haemophilia in France.[510]

381. In autumn 1983, Professor Soulier (then director of CNTS) published an article in the French Review of Transfusion and Immuno-Haematology, stating that the mortality rate for AIDS in the United States was approaching 100% and that the recently completed preliminary phase of the Cochin study had found that 4 out of every 1,000 Parisian donors were at risk for the disease, and that the use of volunteer donors was no assurance of safety given the large pool sizes.[511] He and others recommended that patients with haemophilia should be treated with cryoprecipitate. The recommendation was not taken up by those treating people with haemophilia in France.[512]

382. On 13 March 1984, the CNTS sponsored a scientific conference at which Dr Couroucé (a physician with the CNTS) reported there was "a high incidence" of HIV antibody amongst 133 people with haemophilia tested at the Pasteur Institute. These results were not published or made known to the Ministry of Health or the French Association of Haemophiliacs.[513]

383. In May 1984 Travenol repeated its offer to sell CNTS heat treated factor concentrates. Thereafter CNTS accepted occasional imports of this product.[514]

384. In September 1984 the results of a study of seropositivity among 245 people with haemophilia conducted by Dr Couroucé and Dr Rouzioux, a virologist at

[509] KREV0000001 at p.820.
[510] KREV0000001 at p.820.
[511] KREV0000001 at p.838
[512] RLIT0001907 at p.17.
[513] KREV0000001 at p.838.
[514] KREV0000001 at p.827.

the Claude Bernard Hospital in Paris, were released. The study demonstrated that seropositivity levels increased with frequency of treatment and that French factor concentrates caused HIV infection.[515]

385. On 11 October 1984, the French Association of Haemophiliacs made a public statement that "*we should continue to place strong trust in our physicians and in the products they prescribe…there is no miracle product in other countries.*"[516]

386. In December 1984 the CNTS stated that it intended to move to heat treated products as soon as possible, in light of the then reported incidence of 43% LAV antibodies in people with haemophilia and two cases of AIDS in haemophilia patients treated with local Factor IX.[517]

387. In addition, in December 1984, Professor Allain of the CNTS finalised a study begun in April 1984 of 18 people with haemophilia treated exclusively with a commercial heat-treated product. They had not sero-converted.[518]

388. On 16 January 1985 Dr Allain wrote to the President and Director General of the Paris blood bank urging the immediate heat treatment of plasma or the importation of heat-treated products.[519] He said as follows:

"The problem of the transmission of the LAV virus by coagulant fractions and the probable consequence of this, AIDS, is now a major concern of public health. A recent study which I have the privilege of co-ordinating has shown that in 1983 – 1984 47 per cent of French haemophiliacs were carriers of an LAV trace and that French products were infective for 35 per cent of the subjects receiving factor VIII or human factor IX complex."

389. In January 1985, a test of Parisian blood donors showed that five of every 1,000 were HIV-positive. In March 1985 this was drawn to the attention of the

[515] KREV0000001 at p.838.
[516] KREV0000001 at p.838.
[517] HCDO0000273_065.
[518] RLIT0001907 at p.20.
[519] RLIT0001907 at p.10.

Director-General for Health in a letter which stated that *"it is likely that all the blood products made from pools of donors in Paris are now contaminated."* [520]

390. On 7 May 1985, Dr. Michel Garretta, then-director of CNTS (Professor Soulier's successor), notified the LNS that half of French people with haemophilia receiving transfusions were HIV positive and that every three months of delay in instituting protective measures *"means the eventual death of five to 10 haemophiliacs and some of the person close to them."* He concluded *"it is a matter of the utmost urgency to stop the spread of this contamination among haemophiliacs and their families."*[521]

391. It was known by CNTS by at least May 1985 that all the plasma pools were liable to be contaminated with HIV.[522]

392. At a meeting at the end of May 1985 a decision was made to continue distributing non-heat-treated factor concentrates until it was prohibited. At a meeting on 20 June 1985, CNTS decided to continue to use unheated products until the stocks were depleted.[523]

393. A letter was circulated to every member of the French Association of Haemophiliacs on 25 June 1985 stating that the level of LAV infection in French people with haemophilia was high, that all French products were potentially infectious, that LAV blood tests were available, that all people with haemophilia must be tested, that seropositive people with haemophilia should take precautions in particular in sexual relations and that seronegative patients must use heat-treated products.[524]

394. A decree issued on 23 July 1985 provided that after 1 Oct 1985 non-heat-treated blood products could no longer be paid for by health insurance, amounting in practice to a prohibition on using them. However untreated stocks from patients' homes and in hospitals were not recalled. Only one treatment

[520] RLIT0001907 at p.16; RLIT0000456 at p.121.
[521] RLIT0001907 at p.11.
[522] KREV0000001 at p.831.
[523] RLIT0001907 at pp.29–31; KREV0000001 at p.831.
[524] KREV0000001 at p.839.

centre in Rouen did this.[525]

395. By May 1986:

a. In terms of the treatment for people with haemophilia, 58.5% of the total Factor VIII treatment was provided by way of cryoprecipitate. No patients were treated solely with cryoprecipitate.
b. 51% of the total Factor VIII concentrate used came from commercial sources, who did not specify the origin of the plasma they used.
c. None of the Factor IX concentrate used came from commercial sources. [526]

Selection of Donors

396. In May 1983 CNTS published a circular about AIDS for distribution to blood donors. This set out who was at high risk of transmitting AIDS. It included a questionnaire for donors to complete, and it asked them questions about their behaviour and whether they were suffering from any symptoms of AIDS.[527]

397. This was followed in June 1983 by a circular from the Direction Generale de la Sante (Directorate General for Health) , with donor screening guidelines which asked all blood centres to practise donor selection by identifying at risk individuals by means of a clinical examination.[528] Donors were also to be given information about AIDS before they donated, and a sample pamphlet was attached to the circular.[529]

398. A survey of blood transfusion centres conducted in February 1984 revealed that AIDS and sexual orientation was not mentioned by over half of the participants to the survey during their blood screening procedures.[530] This survey however needs to be treated with some caution, only half the centres participated in it, and of those, only nine centres stated that they systematically

[525] RLIT0000456 at p.123.
[526] PRSE0003860.
[527] KREV0000001 at p.823.
[528] RLIT0000456 at p.119.
[529] KREV0000001 at p.823.
[530] RLIT0000456 at p.119; KREV0000001 at p.824.

asked questions about the donors' 'private life'. It remains unclear therefore, whether no mention was made of AIDS and sexual orientation, because no questions were not asked that would elicit a response about this, or because there was nothing to reveal.

Prisoners

399. According to the book *AIDS, Blood and the Politics of Medical Disaster*,[531] when the risk of AIDS became known in April 1983, the CNTS immediately stopped its blood collections in prisons followed by collections from those centres that relied on the Parisian Public Hospital administration. However, it did not make the dangers public or advise other organisations against blood donation in locations where it was likely that underlying prevalence rates would be higher.

400. No donor selection processes were introduced in penal institutions in 1983, when they were introduced elsewhere. It does not appear that they were introduced in prisons until mid-1985.[532]

401. In 1984 the number of authorised collections in prisons was increased.[533]

402. In spring 1985 a prison physician reported that 54% of prison donors belonged to risk groups. It was only in the latter part of 1985 that collection of blood in prisons dropped to a tenth of its previous level. Blood collection in prisons was only stopped completely in 1991.[534]

403. Blood collected from prisons accounted for less than half a percent of total national supply until 1985, but those donors were responsible for as much as 25% of the cases of contamination through blood.[535]

Screening donations for HLTV-III

404. No surrogate HTLV-III testing was introduced in France.[536]

[531] RLIT0000456 at p.120.
[532] KREV0000001 at p.824.
[533] RLIT0000456 at p.120.
[534] RLIT0000456 at p.120.
[535] RLIT0000456 at p.121.
[536] KREV0000001 at p.835.

405. On 28 February 1985 the Institute Pasteur submitted an application to the Laboratoire national de la sante for approval of its LAV testing kit. Earlier that month Abbot had applied to have its HTLV-III testing kit licensed. Dr Netter wrote to the Minister of Health suggesting that approval for the Abbott kit should be deferred until the Pasteur kit was approved. This was the decision made at a meeting on 9 May 1985 of Cabinet advisors.[537]

406. On 21 June 1985 the Pasteur testing kit was licensed. On 23 July a ministerial order was issued stating that blood donor testing would be compulsory on 1 August 1985. The following day the Abbott kit was licensed for use. The testing of blood donors began on 1 August 1985.[538]

407. The arrangements in place for donor screening were as follows:
    a. The ELISA direct screening test was used, with the Western Blot as the confirmatory test. [539]
    b. Pursuant to a circular in October 1985, donors were to be informed if they were seropositive.[540]
    c. There were no community testing sites in France until 1987.[541]

408. By May 1986 1.4 million donations had been screened. 972 (or 0.68) had been found to be positive. The following arrangements were in place:
    a. In the event that a donor tested positive, (s)he would be seen by a physician at the blood transfusion centre and then followed up by a hospital specialist.
    b. There was no anonymous community testing for HLTV-III. During discussions at the meeting of the Council of Europe's Committee of Experts on Blood Transfusion and Immunohaematolgy in May 1986 as to whether the lack of such facilities had led to the increased frequency of positive donations in France, France confirmed that at the commencement

[537] KREV0000001 at p.836.
[538] RLIT0000456 at p.121; KREV0000001 at p.836.
[539] PRSE0003860.
[540] KREV0000001 at p.837.
[541] RLIT0000456 at p.122.

of testing in August 1985, there had been an influx of new donors who had not returned on recall for a further donation.[542]

409. In a report dated September 1989 of a meeting of the Council of Europe Committee of Experts on Blood Transfusion and Immunohematology in May 1989, it was reported that a look back programme conducted in Paris had found that 25% of previous donations of donors found out one year later to be seropositive had turned out to transmit HIV to recipients despite negative serological status at the time of donation. Further "*according to a mathematical stimulation study carried out in Paris HIV infected but seronegative individuals donating blood during the window period could represent up to 20-30% of the total number of infected donors*." The Committee recognised this evidence was cause for concern and stressed the need for "*more effective mobilisation and policies of information and education of the public in general and prospective blood donors in particular*".[543]

410. In 1991/1992 criminal prosecutions were brought in relation to contaminated blood against the former director of the CNTS, Michel Garretta, his assistant Jean-Pierre Allain, Professor Roux, the Director General of Health and Dr Netter, director of the Laboratoire national de la sante:

a. The primary issues in the trial were the delay in manufacturing heat-treated concentrates and the distribution between March and October 1985 of non-heat treated products from CNTS which were known to be contaminated with HIV.
b. Michel Garretta and Professor Allain were convicted in October 1992 for having failed to prevent the infection of people with haemophilia caused by the distribution of potentially contaminated factor concentrates. Garretta was given a 4 year jail sentence and Allain was sentenced to four years with two years suspended.[544] Allain's sentence remained unchanged after his appeal in June 1994.[545]

[542] PRSE0003860.
[543] DHSC0002509_051 at p.8.
[544] RLIT0001907.
[545] RLIT0001908.

c. Professor Roux was accused of having failed to stop the distribution of unheated clotting concentrates and Dr Netter was charged with failing to authorize the marketing of the Abbot HIV testing kit, instead giving priority to the French produced Pasteur kit. Professor Roux received a suspended sentence of four years imprisonment. Dr Netter was acquitted.
d. CNTS was ordered to pay damages of US$1.8 million.[546]

411. In February 1999, three former French cabinet members were put on trial before the Court of Justice of the Republic, a court created to judge government ministers accused of wrongdoing while discharging their duties. Former Premier Laurent Fabius, Social Affairs Minister Georgina Dufoix and Health Minister Edmond Herve were accused of manslaughter for their part in the management of France's blood banking system in the 1980s. It was alleged that they delayed screening blood for HIV until a French test became available.[547] Laurent Fabius and Georgina Dufoix were acquitted, Edmond Herve was convicted but received no sentence.[548]

Prevalence

412. According to a draft report, *Acquired Immunodeficiency Syndrome, An Assessment of The Present Situation in the World*, dated 12 December 1983, by 20 October 1983 France had reported 94 cases of AIDs to the WHO. France reported the number of cases under each "Year of Diagnosis" as before 1979 (6), 1979(1), 1980 (5), 1981 (5), 1982 (30) and 1983 (47).[549]

413. In October 1983, the World Health Organization reported that France had the highest number of cases of AIDS among fifteen European nations. The *Bulletin épidémiologique hebdomadaire* reported that, by the end of 1984, AIDS cases were increasing at a rate of four per week, and that 90 per cent of AIDS cases diagnosed in France were in Paris. [550]

[546] RLIT0000456 at p.134.
[547] KREV0000001 at p.845.
[548] RLIT0000456.
[549] CBLA0001775 at p.35.
[550] KREV0000001 at p.820.

414. At the end of 1984 the preliminary antibody test results became available and it was clear that a majority of people with haemophilia in France were seropositive. This was known as the Cochin study. By 12 December 1984, 2,000 donors had been tested. They found AIDS antibodies in six out of every 1,000 Parisian blood donors. This gave rise to an estimate that 2,500 patients each year would become infected from contaminated blood donated by French donors.[551] (The numbers of people with haemophilia in France who regularly received blood products are set out below at paragraph 415).

415. In December 1984 the results of LAV testing in different groups of people with haemophilia were finalised.[552] The results were as follows:

a. French people with haemophilia had an overall infection rate of 47%.
b. French people with haemophilia treated with local products had an infection rate of 30%.
c. French people with haemophilia treated with local and foreign clotting factors had an infection rate of 60%.
d. Patients treated with autoplex, Feiba and PPSB local[553] had an infection rate of 17%.
e. People with haemophilia B treated exclusively with local Factor IX concentrate had an infection rate of 43%.

416. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[554] The information as to prevalence in France is as follows:

a. As at March 1986, the population of France was 56 million.
b. There had been 707 cases of HTLV-III and 320 people had died. Of these cases, 29 had been infected via transfusion (excluding people with haemophilia).

[551] KREV0000001 at p.828.
[552] HCDO0000273_065.
[553] A plasma derivative that contains the vitamin K-dependant clotting factors.
[554] PRSE0003860.

c. Of the 3,444 haemophilia A patients in France, 2,583 received regular treatment, 1,733 had been tested for HTLV-III and 887 (or 51%) had tested positive. Of those 11 had developed AIDS and 52 had AIDS related complex.
d. Of the 608 haemophilia B patients, 457 of them received regular treatment. 329 had been tested and 152 (50%) had tested positive for HTLV-III. Of which 4 had developed AIDS and 17 AIDS related complex.

417. The European Centre for the Epidemiological Monitoring of AIDS recorded that as of 30 September 1990, 167 people with haemophilia and 662 transfusion recipients were reported as having AIDs in France.[555]

418. By May 1993, around 300 people with haemophilia had died as a result of contracting AIDS from contaminated blood products.

419. Between 1985 and 1993 there were 1,926 cases of blood related AIDS, an incidence rate of 3.2 per 1,000,000 each year – significantly higher than the next highest country, Spain.[556]

420. On 31 March 1995, France accounted for 56.2% of the recorded cases of AIDS in the European Union.[557]

421. As at December 1996, 1,732 cases of AIDS including 89 paediatric cases had been reported as a result of transfusions. 543 people with haemophilia, including 51 children (out of a population of 5,000) had developed AIDS because of their treatment with factor products. 187 heterosexual cases of AIDS were linked to the blood-borne HIV infection of sexual partners. HIV infection was more widespread, estimated to account for between four and six thousand cases of infection due to blood or blood products. More than 1,200 (40%) of the 3,000 people with severe haemophilia were infected.[558]

[555] NHBT0010038_001 at p.25.
[556] KREV0000001 at pp.817-818.
[557] RLIT0000456 at p.138.
[558] RLIT0000456 at p.124.

422. The figures given in the Krever report are slightly different. This provides that by the end of 1996:[559]

a. More than 1,250 of the country's 4,000 people with haemophilia became infected with HIV, with 527 reported cases of AIDS.

b. There were 1,662 reported AIDS cases amongst transfused patients.

Australia

Knowledge of risk

423. The first diagnosis of AIDS in Australia was made in Sydney in December 1982 but not reported until April 1983.[560]

424. On 11 June 1983 the Medical Journal of Australia published an article noting that the epidemiology "*suggested a transmissible agent spread in a way similar to that of hepatitis B infection…transmission via blood and blood products seems likely….. It is now recommended that individuals at risk should not donate blood*".[561]

425. The National Health and Medical Research Council issued public advice in October 1983 stating that there was no evidence that blood products in Australia were at risk of transmitting AIDS.[562]

426. In May 1985 there were two reported cases of AIDS among people with haemophilia.[563]

Donor screening

427. In February 1983 members of the Haemophilia Federation asked for the introduction of voluntary donor forms but were told by the Blood Transfusion Service (operating through the Red Cross) that questions about sex would embarrass female donors and that Australia's blood supply was safe.[564]

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[559] KREV0000001 at p.818.
[560] RLIT0000456 at p.263; KREV0000001 at p.799.
[561] PJON0000172_013; KREV0000001 at pp.799-800.
[562] RLIT0000456 at p.265.
[563] KREV0000001 at p.801.
[564] RLIT0000456 at p.263.

428. In May 1983 the director of the Sydney Blood Transfusion Service publicly called for homosexual men to avoid donation and said in a television interview that it was "*a virtual certainty that AIDS was in the blood supply*".[565] In response, the chairman of the national blood transfusion committee said:[566]

> *"The position will continue to be kept under close review but it is considered that there is no cause for alarm at present and it is not felt necessary to request any particular group in the community outside NSW (New South Wales) to refrain from donation blood."*

429. The National Blood Transfusion Service recommended on 1 June 1983 that information sheets be issued at donation centres asking for abstention by sexually active homosexual or bisexual men, intravenous drugs users and the sexual partners of these people. Also recommended was the provision of a leaflet to educate the public about AIDS.[567] Steps were taken by all states to encourage voluntary self-exclusion with the use of leaflets, although this was not done simultaneously. The wording on the leaflets identifying those who should self-exclude was not the same across the states.

430. In the late summer of 1984, a blood donor tested positive for HTLV-III. He was a gay man and was aware of the blood transfusion service request that those in high risk groups should self-exclude but had donated because he did not consider himself promiscuous.[568] According to the Krever report '*blood banks immediately tightened their criteria for donors, and excluded all men who had had a homosexual contact in the preceding five years'*. Sydney BTS began to require donors to sign a form declaring they were not a member of a high-risk group, but this was not adopted at this stage in other states. [569]

431. On 15 November 1984, the Queensland government announced that three infants had died after receiving "*contaminated blood from a homosexual donor*".[570] At a meeting

[565] RLIT0000456 at p.264; KREV0000001 at p.803.
[566] KREV0000001 at p.803.
[567] RLIT0000456 at p.265; KREV0000001 at p.804.
[568] KREV0000001 at p.800.
[569] RLIT0000456.
[570] Reported in the Lancet NHBT0112288_003.

on 19 November of federal and state ministers, it was agreed that there should be a uniform donor declaration for all blood banks. Legislation across all states imposing criminal sanctions for false declarations by donors was enacted.[571]

432. After 1 May 1985 (when donation screening was introduced – see below), the declarations donors were required to sign concerned their suitability to donate in the knowledge that the blood would be tested for LAV/HTLF-III antibodies and a warning that there were penalties for providing false or misleading information.[572]

433. In February 1992, Dr Gunson made enquiries with other countries about their donor leaflets '*to ensure that donors with high risk activities which may give an increased risk of HIV do not donate blood.*'[573] He received a form from the state of Victoria in Australia.[574] This stated:

"DO NOT DONATE BLOOD IF YOU ARE:

- *A Homosexual or Bisexual male*
- *An intravenous drug user*
- *A prostitute*
- *A client of a prostitute*
- *A sexual partner of any of the above."*

434. The leaflet was accompanied by a letter and a declaration that each donor was required to sign to declare that:

(1) I have no reason to believe that I have the Acquired Immune Deficiency Syndrome (AIDS) or carry the virus that causes AIDS;

(2) I am not suffering from night sweats or unintentional weight loss or persistent fever, diarrhoea or swollen glands;

(3) I have not engaged in male-to-male sexual activity on any occasion since 1 January 1980;

[571] RLIT0000456 at p.267; KREV0000001 at pp.802 and 805.
[572] NHBT0009083_009.
[573] NHBT0007305_001.
[574] NHBT0007305_003 at pp.1-3.

(4) I have not injected myself, or been infected with any drug not prescribed by a registered medical practitioner, since 1 January, 1980;

(5) I have not received a blood transfusion or treatment with human blood products within the past twelve months;

(6) Neither my spouse nor any other sexual partner comes within the categories described in paragraphs (1), (2), (3), (4) and (5);

(7) I have not been tattooed within the past twelve months;

(8) I have not in the past six months had jaundice or hepatitis, or been in close contact with a case of those illnesses.

Screening donations

435. The first use of diagnostic testing for post-transfusion AIDS of an Australian blood donor was in July 1984, when a rudimentary test was carried out in San Francisco on a donation.[575]

436. On 5 October 1984 surrogate HTLV-III testing in the form of hepatitis B core testing was implemented at the New South Wales blood transfusion service.[576]

437. The decision to introduce screening of donations was made on 19 November 1984 by a meeting of the state and federal ministers at a meeting a matter of days after the announcement of the death of three babies from transfusion related AIDS (see above).[577]

438. Australia was the only non-US participant in the US Food and Drug Administration's evaluation of five diagnostic test kits, which took place from October 1985 to January 1986.

439. According to the European Health Committee report on AIDS Developments in Member States, Finland and Australia, HTLV-III screening began in mid-April 1985 simultaneously in blood centres and public health centres (i.e. community centres) in each state.[578] According to the Krever report it was not fully implemented in all blood banks until May 1985.[579] Australia used the ELISA direct screening test, with the

[575] KREV0000001 at p.800; RLIT0000456 at pp.265-266.
[576] KREV0000001 at p.808.
[577] KREV0000001 at p.802.
[578] NHBT0009083_009.
[579] RLIT0000456 at p. 268; KREV0000001 at p.808.

Western Blot and unspecified other tests as confirmatory tests.[580]

440. Donors who were ultimately declared positive following confirmatory testing, were informed. [581] They would be seen by a physician at the blood transfusion centre, and then followed up by a specialist physician.[582]

441. By May 1986 Australia had screened 556,146 donations. 26 had tested positive (0.005%).[583]

Risk reduction measures taken with respect to blood and plasma

442. On 18 October 1984 Australia's national blood transfusion service AIDS working group recommended heat sterilization be urgently introduced and that all supplies of anti-haemophiliac factor be tested, following the recent announcement at the CDC in Atlanta.[584] A working party on heat treatment of Factor VIII was convened on 2 November 1984.

443. From February 1985 all Factor VIII concentrate manufactured by CSL was heat treated at 60 degrees centigrade for 72 hours. Unused non-heat treated product was returned to CSL to be heat treated, but some non-heat treated products were still being used in early 1985.[585]

Prevalence

444. A survey carried out by the World Haemophilia AIDS Centre reported that, in a set of survey responses as of 25 September 1984, out of 1,105 people with haemophilia who were tested for AIDS in Australia there were no AIDS cases, but one case of Aids Related Complex.[586]

[580] PRSE0003860.
[581] NHBT0009083_009.
[582] PRSE0003860.
[583] PRSE0003860.
[584] RLIT0000456 at p.266.
[585] KREV0000001 at p.807; NHBT0009083_009.
[586] BAYP0000024_068.

445. In 1984, out of an estimated 1,500 people with haemophilia, about 900 were treated with blood products. 264 of them received products contaminated with HIV. Studies of stored sera showed the developing prevalence of HIV antibody: 1981 – 0%; 1982 – 9.8%; 1983 – 11.9%; 1984 – 31%.[587]

446. The National Centre in HIV Epidemiology and Clinical Research published a table in 'An Epidemiological Assessment of the HIV Epidemic in Australia' in 1996 which provided that in Australia, the following cases of transmission of HIV by transfusion occurred year by year: [588]

Year of infection	Number (%)
Before 1981	12 (6)
1981	20 (11)
1982	32 (17)
1983	54 (29)
Jan – Nov 1984	51 (27)
Nov 1984 – May 1985	4 (2)
Not known	16 (8)
Total	189 (100)

447. A Council of Europe report stated that by May 1985, two people with haemophilia had tested positive for AIDS, and there were eight transfusion associated cases.[589]

448. An extract of the Berne Conference report from 28 to 31 May 1986, dealing with AIDS, sets out the replies from the attending countries to a questionnaire sent out by Dr Gunson.[590] The following information about the prevalence of HTLV-III in Australia is set out:

a. As at March 1986, the population of Australia was 15.6 million.
b. There had been 172 cases of HTLV-III of whom 79 had died.

[587] RLIT0000456 at p.269.
[588] As reproduced in RLIT0000456 at p.269.
[589] NHBT0009083_009 at p.9.
[590] PRSE0003860.

c. 19 of these had been infected via blood transfusions (excluding people with haemophilia).
d. Of the 1,500 people with haemophilia A in Australia, 500 were in receipt of regular treatment. 50% of those with haemophilia A had been tested for HTLV-III. 30% were positive. Three had developed AIDs.
e. There were 150 people with haemophilia B, but no information as to whether or not they had been tested for HTLV-III was provided.

449. In an advice to the Australian Government Solicitor for the HIV litigation in the 1990s in the Supreme Court of Victoria, it was reported that by 1990 "*Approximately 330 Australian haemophiliacs had either contracted AIDS or HIV. Most of these have HIV and have not yet developed full blown AIDS. This represents approximately 75% of the haemophiliacs in Australia.*"[591]

450. According to the Krever report, in April 1992 the World Federation of Haemophilia reported that of the approximately 1,570 people with haemophilia in Australia, 1,431 had been tested for HIV. [592] 260 had tested positive (18%) and 79 (5.5%) had developed AIDS. 55 had died. It is recorded that *"Because Australia has long had a policy of self-sufficiency in blood products, these infections are attributed solely to the use of factor concentrates manufactured domestically from Australian plasma."*

451. According to the Krever report, by the end of 1993, 127 cases of transfusion related AIDS had been reported, representing 2.4% of the AIDS cases in Australia.[593]

452. A look-back programme was initiated in 1985, initially in New South Wales and then extended nationally, which may have led to particularly high pre-1985 recorded cases in comparison to other countries. By the end of 1995 a total of 172 blood-transfusion cases had been identified nationally, all with infection dates no later than May 1985.[594]

[591] CBLA0000069_035 at p.2.
[592] KREV0000001 at p.799.
[593] KREV0000001 at p.799.
[594] RLIT0000456 at p.269.

453. From April 1985 to December 1996, out of 11 million donations tested for HIV-1 antibody, 87 were found to be positive. No instance of HIV transmission from blood or blood products had been identified since April 1985.[595]

Prevalence comparison tables

454. Between 19 and 21 October 1983, a meeting co-sponsored by the Danish Cancer Society, the World Health Organisation, and the European Organisation for Cooperation in Cancer Prevention Studies took place in Aarthus in Denmark. In the full report of that meeting there are some tables showing rates of infection in various countries. [596]

Table of AIDS cases reported to WHO from European countries as of 20 October 1983, arranged by country and year of diagnosis:[597]

Country	<1979	1979	1980	1981	1982	1983	Total
Austria						7	7
Belgium			2	4	8	24	38
Czechoslovakia					1	1	2
Denmark			1	2	4	6	13
Finland						2	2
France	6	1	5	5	30	47	94
Germany (FDR)	1	1			7	33	42
Ireland						2	2
Italy	1				2		3
Netherlands					3	9	12
Norway						2	2

[595] RLIT0000456 at pp.268-9.
[596] SHPL0000344_010.
[597] SHPL0000344_010. The German Democratic Republic, Greece, Hungary, Luxenberg, Poland, USSR and Yugoslavia reported no cases. No information was received from other countries.

Spain			1	1	4		6
Sweden					1	3	4
Switzerland			2	3	5	7	17
United Kingdom				2	5	17	24

455. A different table in that report showing the breakdown of the cases according to the risk group the person belongs to, suggests that (a) this information was collected in respect of 148 of the 200 positive people, and (b) of those, the only person with haemophilia were one in 1982 (in Germany) and five in 1983 (one in Austria, one in France, two in Spain and one in the UK).[598]

456. There is a table in 'Plasma Quarterly' (the Winter 1984 edition) which provides data that as at 15 July 1984 according to the WHO Health Statistics Annual, Geneva, the rates were as follows:[599]

Country	**Numbers**	**Rates per Million**
Denmark	28	5.5
France	180	3.4
Federal Republic of Germany	79	1.3
Greece	2	0.2
Italy	8	0.1
Netherlands	21	1.5
Spain	14	0.4
Sweden	7	0.8
Switzerland	28	4.4
United Kingdom	54	1.0

[598] See also PRSE0003037.
[599] BAYP0005567 at pp.19 and 21.

457. The European Health Committee produced a Report on AIDS Developments in Member States, Finland and Australia, to accompany its main Meeting Report dated 28 to 31 May 1985 reported that to date:[600]

a. In Belgium only 3% of people with haemophilia were anti-HTLV-III positive 'these cases being the result of imported concentrates'. No cases of AIDS from transfusion had been identified in people with haemophilia.
b. In Denmark 40 – 50 cases of AIDS had been diagnosed out of 5 million inhabitants. None had been transfusion associated.
c. In Australia, there were 8 transfusion related and 2 people with haemophilia AIDS cases out of 78 cases notified up to 9 May 1985. The incidence of anti-LAV/HTLV-III in people with haemophilia subject to screening was 28% in a country which used no commercial concentrates.

458. That same report included a table setting out the number of AIDS cases identified up until May 1985:

Country	**Total Number**	**People with haemophilia**	**Transfusion associated**
Austria	Start IV/83 till V/85:15 (12 died)`	2 registered	
Belgium	81	0	0 in Belgium (4 in Africa)
Cyprus	0	0	0
Denmark	45 – 50	0	0
France	350	8 (together with transfusion)	
Federal Republic of Germany	180	5	0
Greece	8	1	
Iceland	0		

[600] NHBT0009083_009.

Ireland	5 (2 deceased)	1	
Italy	39		1
Luxembourg	1	0	No
Malta	0		
Netherlands	52	0	1
Norway	8	0	0
Portugal	5	1	0
Spain	14	3	3
Sweden	22 (11 died)	1	0
Switzerland	52	0	0
UK	157	5	2 (transfused outside UK: 1 in USA and 1 in Dubai
Australia	76	2	8
Finland	5	0	0

459. In September 1990 the Public Health Laboratory Service Aids Centre and the Communicable Diseases (Scotland) Unit released the following information concerning European rates of AIDS:[601]

Country	**Number**	**Rate per million**
Albania	0	0
Austria	474	62.1
Belgium	764	76.9
Bulgaria	7	0.8
Czechoslovakia	24	1.5
Denmark	663	129
Finland	71	14.3
France	9,718	173
German Dem Rep	25	1.5
Germany Fed Rep	5,266	84.7
Greece	375	37.4

[601] NHBT0008408_037.

Hungary	42	4
Iceland	14	56
Ireland	161	45.9
Israel	125	27.2
Italy	7,576	131.7
Luxembourg	30	79.6
Malta	15	42.9
Monaco	4	142.9
Netherlands	1,443	97.2
Norway	176	41.6
Poland	43	1.1
Portugal	481	46.6
Romania	999	43.1
San Marino	1	43.5
Spain	7,047	181.2
Sweden	487	57
Switzerland	1,497	225.1
Turkey	36	0.6
United Kingdom	3,798	66.3
USSR	40	0.1
Yugoslavia	147	6.2

460. In November 1990 EAGA set out the number of AIDS cases reported in Europe as of November 1990:[602]

Country	**Number**
Albania	0
Austria	474
Belgium	764
Bulgaria	7
Czechoslovakia	24

[602] NHBT0008408_038.

Denmark	690
Finland	71
France	9,718
Germany Fed Rep	5,380
Greece	375
Hungary	48
Iceland	14
Ireland	161
Israel	125
Italy	7,576
Luxembourg	30
Malta	15
Monaco	4
Netherlands	1,456
Norway	180
Poland	47
Portugal	492
Romania	999
San Marino	1
Spain	7,047
Sweden	487
Switzerland	1,497
Turkey	36
United Kingdom	3,798
USSR	40
Yougoslavia	147
Total	41,403

461. In September 1992 WHO reported on the number of people with haemophilia/coagulation disorder who had been diagnosed with AIDS as well as the number of people who had been infected via a blood transfusion in Europe:[603]

[603] NHBT0019285_006.

Country	Haemophilia/coagulation disorder		Transfusion recipient **	
	N	%***	N	%***
Austria	42	5.1	21	2.5
Belgium	5	0.4	83	6.8
Denmark	21	2.0	19	1.8
Finland	1	0.9	3	2.7
France	308	1.4	1,150	5.4
Germany	358	4.0	174	2.0
Greece	45	6.5	46	6.7
Iceland	0	0.0	2	9.1
Ireland	20	6.8	0	0.0
Italy	178	1.2	202	1.4
Luxembourg	2	3.6	2	3.6
Malta	9	36.0	0	0.0
Netherlands	39	1.7	33	1.4
Norway	7	2.5	15	5.3
Portugal	38	3.7	48	4.6
Spain	427	2.7	175	1.1
Sweden	30	4.0	38	5.1
Switzerland	18	0.7	34	1.3
Turkey	4	4.5	12	13.5
United Kingdom	328	5.0	79	1.2

** Includes recipients of blood transfusion or tissues

*** % of total cumulative AIDS cases per country

Knowledge of risk: Non A, Non B Hepatitis / Hepatitis C

462. The Council of Europe Committee of Experts in Blood Transfusion and Haematology met in May 1987. A report was prepared, *Non A Non B Hepatitis – Testing of Blood*

for Indirect Evidence of Infectivity, which was a *"synthesis of replies from members"* to a questionnaire about non A, non B hepatitis. In the introduction, it was noted that the "*replies indicated that this issue is, in general, given careful consideration by most blood transfusion services. The general impression given is that the incidence of non A, non B is low, but varies widely between different region. The value of "surrogate" tests such as ALT and anti-HBc has been studied by various groups but there is doubt as to their cost-effectiveness. Professor H. Weise remarked that ALT testing had been used in the Federal Republic of Germany for more than 20 years, and the reduction of NANB hepatitis was estimated to be 29%, although no controlled studies had been carried out."* [604]

463. The working group found:

"Many factors are involved in the incidence of transfusion associated NANB hepatitis. There is a geographical variation with a tendency for a higher prevalence in Southern European Countries. However, in all countries blood transfusions are transmitting NANB hepatitis, most commonly recognised by a persistent elevation of liver enzymes. The disease may run a symptomless course, but in some cases there is chronic disease resulting in microscopical evidence for cirrhosis and very occasionally the disease is fulminating and rapidly fatal. The argument for introducing tests to reduce the incidence of NANB hepatitis following blood transfusion has been supported by the prediction that up to 10% of infected patients with persistently elevated liver enzymes will develop cirrhosis."[605]

However, the report went on to raise a question as to whether a *"healthy carrier state"* might exist in light of the hepatitis epidemiology in the USA.

464. Recognising that there was no specific test for NANB hepatitis, the report stated: "*The only possibility for reducing the incidence of transfusion associated NANB hepatitis appears to be the use of non-specific tests. In this context, ALT and anti-HBc testing of blood donors has been proposed and it has been predicted in the USA that this will lead to a 35% reduction in the incidence of the disease, but not to its prevention…Routine screening of blood donors for ALT and anti-HBc has started in the USA. In European countries ALT screening was used in Switzerland for a short period in the 1950's, but*

[604] NHBT0008816_002 at p.1.
[605] NHBT0008816_002 at p.4.

was discontinued. It has been undertaken in the Federal Republic of Germany and some regions in Italy since 1965, but it has not been possible to evaluate its effectiveness in the prevention of transfusion associated NANB hepatitis. A prospective study in two Centres in France has shown that ALT values significantly correlated with the transmission of NANB hepatitis and their data confirmed that of the USA. In Sweden, longitudinal ALT tests on plasmapheresis donors showed that the ALT value varied within one and the same individual which limited its value."

465. The Report concluded that:

"*8.1 The use of non-specific markers for the purpose of reducing the incidence of transfusion associated NANB hepatitis and its possible value as a Public Health measure remain controversial issues.*

8.2 If a stance is taken that blood should have maximum safety then the tests would be introduced, but benefits derived from this testing would not be uniform throughout every country. Also, in a given country, there is no guarantee that there will be a significant reduction in the transmission of NANB hepatitis. The introduction of non-specific tests could lead in some countries to a severe depletion of blood donors which may compromise the blood supply and this is a factor which must be taken into account….

8.5 The Committee cannot give a general recommendation on the routine introduction of non-specific tests for evidence of NANB infectivity of blood donors. Individual countries will have to assess the situation locally and decide on appropriate action to take."[606]

466. The responses to the questionnaire were also tabulated.[607] The relevant information can be summarised as follows:

Country	Summary of information provided by country
Spain	Screening for ALT and anti-HBc was not compulsory, although some centres were performing ALT tests. An inquiry into the

[606] NHBT0008816_002 at p.6.
[607] NHBT0000061_023.

	incidence of NANB hepatitis was in progress.
Belgium	Blood donations were not routinely screened for ALT and anti-HBc, but donations by plasmapheresis were tested for both. The incidence of post-transfusion hepatitis was 1-2%, climbing to 50% after multiple transfusions. Belgium considered that the introduction of additional testing was justified and that would be in place within months. At that time a prospective study was being carried out to assess the incidence of post-transfusion hepatitis after ALT and anti-HBc testing, the results of which would help to decide on routine testing.
Denmark	Blood donations were not routinely screened for ALT or anti-HBc. Transfusion associated NANB cases were reported as 2 in 1983, 1 in 1984 and 6 in 1985. No action was being taken to determine whether the tests should be performed, and tests were unlikely to be introduced "*unless the number of registered cases of transfusion-associated hepatitis NANB increases significantly*".
Finland	Finland indicated it was not testing all blood donations for ALT or anti-HBc, although they were considering whether additional tests needed to be introduced. Numbers of infections were not available; a study to determine incidence of post-transfusion NANB was planned as earlier studies were not valid *"due to self-exclusion of AIDS risk groups."*
Germany	Germany declared that blood donations were routinely screened for ALT, but not for anti-HBc. ALT testing had been compulsory since 1968. The incidence of post-transfusion hepatitis was approximately 3.6%. Germany indicated it would consider whether the introduction of additional testing was justified after controlled studies of the effect of anti-HB negative vs positive units and that several scientific societies including the Federal Board of Health were evaluating the situation. In answer to the question "*do you consider that the tests will be introduced and on what timescale*?" Germany answered: "*Yes, but probably not before 1988 so as to solve the economic problems and the need*

	to discard > 6% of blood units".
Italy	ALT testing was mandatory but Anti-HBc testing was not routinely performed. The prevalence of post transfusion hepatitis infection was reported to be 10-18%. Italy reported that the introduction of additional tests was justified, but made no indication about what action was being taken or when it would be progressed.
Netherlands	Blood donations were not routinely screened for ALT or anti-HBc. The yearly incident of post-transfusion NANB hepatitis was "*unknown but presumably low. A prospective study is underway*". No decision was to be taken on whether increased safety justified the introduction of additional tests until the results of the study were known, "*probably early 1987*" but "*the first impression is that the incidence is low and that the introduction of additional tests would be of little value*."
Norway	Not routinely screening its donations for ALT or Anti-HBc. As to the incidence of post-transfusion NANB hepatitis: "*the exact incidence is unknown, but it must be very low, not a single verified case has been reported since 1980 when some cases were reported in haemophiliacs. They had received commercial factor VIII preparation produced in a foreign country during a short period of time when self sufficiency was not ensured*".
Iceland	Iceland declared that blood donations were not routinely screened for ALT or anti-HBc. No information was provided about the incidence of post-transfusion hepatitis or introduction of testing.

Sample countries: Knowledge of, and response to, Hepatitis C

Netherlands

467. At a meeting of the European Health Committee's Committee of Experts on Blood Transfusion and Immunohematology in 1988, the Netherlands reported that "*no routine testing with respect to ALT and anti-HBc was being performed. A prospective study of more than 300 coronary by-pass surgery patients (average transfusion of 6/7 units) has shown one in 750 donations to be implicated in transmission of NANB hepatitis. An Advisory Committee is to consider introducing routine screening.*"[608]

468. In a draft witness statement, Dr van Aken, Medical Director of the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam, writing in 1990 stated that hepatitis C testing had been introduced at one centre on a trial basis and would be introduced at all clinics after 1 November 1990. It was expected that testing of plasma delivered to the CLB for fractionation was expected to be introduced after testing at the clinics had been implemented. [609]

469. In a report of the Council of Europe Committee of Experts on Blood Transfusion and Immunohaematology dated June 1991, the Netherlands, responding to a survey, indicated that routine testing of blood had been introduced between January and April 1991, but not of plasma for fractionation.[610] However, a 2019 article on chronic hepatitis C infection in the Netherlands states that donor screenings for HCV were not introduced until 1992. The article also records data from another study indicating that 98% of patients treated before 1992 with large pool (i.e. derived from more than 1,000 different donors) non-HCV-safe clotting factor concentrate had been infected with HCV.[611]

470. As at March 2000, the World Federation of Haemophilia estimated that 90% of the population of patients with haemophilia in the Netherlands were infected with hepatitis C.[612]

Germany

[608] NHBT0000018_019 at p.19.
[609] CBLA0000058_036 at pp. 27 and 28.
[610] NHBT0002345 at pp.5 and 6.
[611] RLIT0000463 at p.3.
[612] HSOC0023772 at p.14.

471. In June 1990, a letter from Ortho Diagnostics stated that hepatitis C testing had been approved for donor screening and would be mandatory by the middle of the year.[613] The commencement of testing in July 1990 is confirmed in Germany's response to a Council of Europe survey.[614] Testing of plasma for fractionation was not being undertaken.[615]

472. HCV infection among people with haemophilia is recorded in Germany as being at an 80% infection rate.[616]

473. As at 1 March 2000, the World Federation of Haemophilia reported an estimated 83% of people with haemophilia in Germany were infected with HCV.[617]

Belgium

474. In 1988, it was recorded that *"There was not a uniform policy [regarding ALT testing]. Approximately 25-30% of donations were screened for ALT, with approximately a rejection of 2% donors and a decrease in complications of 5%".*[618]

475. In a Council of Europe survey response, Belgium stated that whole blood had been tested for hepatitis C since July 1990.[619] However, minutes of an ACVSB meeting record that Belgium had already started testing for Hepatitis C in April 1990.[620] In a letter from Ortho, in June 1990, it was said to be mandatory to test all plasma donations for hepatitis C and whole blood testing would be mandatory from 1 July.[621]

476. In promotional material for the Ortho HCV antibody ELISA test, HCV prevalence amongst people with haemophilia was reported to be 71% in Belgium in 1989.[622] The

[613] NHBT0000073_004.
[614] NHBT0002345 at p.4.
[615] NHBT0002345 at p.6.
[616] NHBT0040833 at p.2.
[617] HSOC0026135 at p.15. These infectivity rates are aggregated for both East and West Germany.
[618] NHBT0000018_019 at p.18.
[619] NHBT0002345 at p.4.
[620] NHBT0000072_098 at p.3.
[621] NHBT0000073_004.
[622] NHBT0040833 at p.2.

World Federation of Haemophilia reported that in 2002, nearly 97% of the Belgian population with haemophilia/VWD were HCV-infected.[623]

Denmark

477. Shortly after hepatitis C was identified in 1989, several Danish blood banks identified trial screening programmes and other blood banks expressed strong interest in undertaking screening. However, the county health authorities who were responsible for blood banks were unwilling to allocate the necessary funds. The National Board of Health was unwilling to fund screening from the central state budget, at least in part because of the quality of the early HCV tests. [624]

478. In correspondence dated 20 June 1990, Ortho Diagnostics reported that two major centres screened all blood donations for HCV, equating to 25% of blood donations in Denmark.[625]

479. In June 1991 anti-HCV screening was introduced nationally.[626]

480. By this point heat treatment had significantly reduced the risk to people with haemophilia and the measure was seen as protective of patients receiving whole blood transfusion which was not heat treated.[627] No data was provided to the Council of Europe Committee in 1991 regarding whether any anti-HCV testing of plasma for fractionation was being undertaken.[628]

481. In response to the risk of HCV, unscreened product was entirely withdrawn from the market by March 1992, at a cost of $4.2 million.[629]

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[623] HSOC0026135 at p.3.
[624] RLIT0000456 at p.198.
[625] NHBT0000073_004.
[626] NHBT0002345 at p.4.
[627] RLIT0000456 at p.198.
[628] NHBT0002345 at p.6.
[629] RLIT0000456 at p.199.

482. The Danish Haemophilia Society estimated that 177 people with haemophilia were infected with HCV through the use of contaminated blood products between the 1970s and the late 1980s.[630]

Finland

483. In his evidence to the Penrose Inquiry, Professor Leikola stated that a study of donors' samples had shown a prevalence of HCV positivity of 0.73%. However, he considered that this was "*possibly slightly higher than in the rest of Scandinavia, which is somewhat surprising considering the clinical background*".[631]

484. In 1990, Professor Leikola et al. published a study which showed that the prevalence of anti-HCV was 50% among 137 Finnish haemophilia patients tested.[632]

485. Routine blood donor screening included anti-HCV screening on a small scale from February 1990, expanded to full scale screening on 1 April 1990.[633] In a sample of 2,700 donors from February 1990, 0.5% were repeatedly reactive in anti-HCV ELISA, falling to 0.3% using the RIBA test. In January to February 1988, 137 patients with bleeding disorders were tested and 50% of the samples were repeatedly reactive with anti-HCV ELISA.[634]

486. At a meeting of the Council of Europe Expert Committee on Blood Transfusion, held in May 1990, the Finnish authorities reported the prevalence of HCV was 0.5% after repeat screening. [635] Approximately 0.3% were positive or indeterminate in the RIBA blot test. All donors with positive or indeterminate RIBA results were deterred from donating, those with negative RIBA tests were recalled for donations.

487. On 6 November 1990 a study was published into post-transfusion hepatitis after open-heart surgery between 1987 and 1989. Of 685 patients, eleven hepatitis cases were

[630] RLIT0000525 at p.1.
[631] PRSE0001810 at p.2.
[632] PRSE0004403 at p.2.
[633] NHBT0027713_121 at p.8. See also NHBT0002345 at p.4.
[634] NHBT0027713_121 at p.8.
[635] PRSE0003672 at p.1. See RCPE0000229_003 cover letter giving date.

recorded representing 1.6% of patients. All were NANB hepatitis. Of the total units of blood transfused, the figure represented 1.3 NANBH cases per 1,000 units. It was stated that this figure was lower than recent studies in Northern Europe, and much less than elsewhere in Europe and North America.[636]

488. The European Committee of Experts on Blood Transfusion and Haematology conducted a survey on anti-HCV tests on blood donations in anticipation of its meeting of 4-7 June 1991. Finland stated that routine anti-HCV testing was carried out on its blood donations and this had been in place partially from 1 February 1990 and fully from 1 April 1990, using the ELISA test. There was a rate of 0.75% intermediary positive and 0.026% confirmed positive results. Donors with a confirmed positive result were counselled and recruited into a study into HCV.[637]

Norway

489. In a letter dated 20 June 1990, Ortho Diagnostics stated their understanding that in Norway all donors were to be tested for HCV with 60% of blood being screened at that time.[638] In a Council of Europe Committee report, it is stated that routine tests for HCV were introduced in Norway between January and June 1990.[639]

490. In a paper published in 1990, the prevalence of HCV antibodies in sera from 266 Norwegians with coagulation factor deficits was assessed to be 41% with the highest rates being found in persons with severe haemophilia A (64%) and B (67%).

Iceland

491. At a meeting of the Committee of Experts on Blood Transfusion and Immunohematology in May 1988 it was reported that no testing for NANB hepatitis was being carried out in Iceland.[640]

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[636] PRSE0004630 at p.4.
[637] NHBT0090373.
[638] NHBT0000073_004
[639] NHBT0002345 at p.5
[640] NHBT0000018_019 at p.19. See also NHBT0002345 at p.4 and p.6 indicating no testing was taking place in 1990.

492. Before screening was introduced, donors were required to complete a questionnaire about drug use.[641]

493. The Icelandic Blood Bank started screening for HCV antibody in the autumn of 1992.[642]

494. During the first year of screening of HCV antibody at the blood bank, eight positive donors were detected. The results of retrospective analysis of stored serum in Iceland showed the first serum which was positive for HCV antibody was from 1984, but there was only one further positive sample from 1985-6 suggesting the virus spread slowly.[643]

Spain

495. In correspondence from Ortho Diagnostic Systems, it appears that in June 1990, HCV testing was mandatory in 50% of the country. In a response to a Council of Europe Committee of Experts on Blood Transfusion and Immunohaematology survey in 1991, Spain was recorded as having introduced hepatitis C testing of blood in October 1990, with 70% of donations being tested. Plasma for fractionation was tested using *"ELISA + RIBA/PCR-".*[644]

Italy

496. Screening for antibodies to hepatitis C virus was routinely performed in some blood banks from October 1990 and became compulsory in August 1991.[645] Plasma for fractionation was tested using *"ELISA + RIBA/PCR-".*[646]

497. In 1989 the incidence of NANB hepatitis post blood transfusion was 4.1 per 1,000,000, falling to 2.9 in 1990. It fell further to 1.4 in 1991, with compulsory testing, and down to 0.3 in 1992 with the introduction of ELISA-II testing.[647]

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[641] RLIT0000465 at p.2

[642] RLIT0000465 at p.2. Hepatitis C "determinations" were started in October 1990, with requests arising from e.g. known i.v. drug use or elevated liver enzymes: at p.2.

[643] RLIT0000465

[644] NHBT0002345 at p.6.

[645] The date in 1991 is unclear: NHBT0002345 at p.5.

[646] NHBT0002345 at p.6.

[647] NHBT0085294_004.

498. In a retrospective study, published in 1994, 788 Italian patients were studied, representing about a quarter of Italian patients with haemophilia A. Of the 788, 708 had been treated for the first time before 1985 (the date when heat treated concentrates were introduced) and 80 patients had first been treated between 1985 and 1991. The study found that the prevalence of anti-HCV was 83% in the first group and 6% in the second.[648]

France

499. A study by Aymard et al. in 1986 found that 6.25% of recipients of blood transfusions developed NANB hepatitis and all these cases were associated with anti-HBc negative blood. None of the anti-HBc positive donations were implicated in transmission of NANB hepatitis.[649]

500. From 15 April 1988, ALT testing was compulsory for all transfusion centres. As at September 1988, anti-HBc screening was not compulsory but was under consideration by the health authorities.[650]

501. In November 1989, Dr Bahman Habibi (Medical and Scientific Director at the CNTS) informed the UK NBTS that the view in France was that since the intermediate products of Factor VIII, which contained immunoglobin, undoubtedly transmitted NANB hepatitis, they probably contained donations which were anti-HCV positive. It was CNTS's view that such donations should be excluded from plasma pools for the preparation of all products. Dr Habibi also said that the FDA recently held a consultive meeting in which advice was given that it was not necessary to exclude such donations from plasma for fractionation. The exact picture of the French/CNTS consensus at this time is therefore unclear.[651]

[648] SBTS0000021_173.
[649] NHBT0116885_002 at p.1.
[650] NHBT0000018_019 at p.19.
[651] NHBT0000188_099.

502. France implemented mandatory testing of all donor blood for hepatitis C in March 1990.[652]

503. A 1996 BMJ article reported that the French Ministry of Social Affairs and Health estimated that between 0.5-1 million people (1-2% of the population) were hepatitis C carriers and that around half of that number had contracted the virus through intravenous drug use or transfusion. According to the French Blood Agency, 95% of patients infected with hepatitis C remained symptom free.[653]

Australia

504. As at September 1988, there was no national policy requiring ALT testing.[654]

505. Routine anti hepatitis C screening was introduced in Western Australia in 1990[655] and was mandatory throughout Australia by at least June 1990.[656]

506. In October or November 1984, CSL adopted a method of heat-treated preparation of Factor VIII which effectively destroyed HBV and HIV.[657] CSL increased heat treatment to a temperature sufficient to eliminate HCV in 1989.[658]

507. In 2004 the Haemophilia Foundation of Australia reported that following treatment with contaminated blood clotting factor concentrates, 85-90% of people with haemophilia had been infected with hepatitis C.[659] The Foundation was of the view that up to 90% of people with haemophilia A and B developed HCV with their first treatments of non-heat-treated factor concentrate.[660]

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[652] NHBT0002345 at p.4. See also NHBT0000073_004.
[653] ARCH0002131 at p.2.
[654] NHBT0000018_019 at p.20.
[655] ARCH0001232 at p.26, referencing *A and Others v National Blood Authority and Others* [2001] EWHC QB 466 (appendix 28).
[656] NHBT0000073_004.
[657] MACK0002565 at p.57.
[658] MACK0002565 at p.58.
[659] MACK0002565 at p.56.
[660] MACK0002565 at p.56.

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