PRESENTATION NOTE ON THE USE OF FACTOR IX CONCENTRATES FOR THE TREATMENT OF PEOPLE WITH HAEMOPHILIA B

Introduction

1. The use of Factor VIII concentrates (and in particular the use of imported commercial Factor VIII concentrates), and the question of what was - or was not - done by way of attempts to achieve self-sufficiency in the UK, have been explored extensively in the Inquiry's hearings through oral evidence and presentations. The use of Factor IX concentrates has not featured as prominently, not least because the UK was largely self-sufficient in relation to Factor IX and there was substantially less reliance on imported commercial concentrates. The purpose of this presentation note is to draw together some of the material which the Inquiry holds in relation to the production and use of Factor IX and the treatment of people with haemophilia B, many of whom were infected with hepatitis and/or HIV in consequence of that treatment.

2. All page references below refer to the electronic page on Relativity.

Haemophilia B

3. Haemophilia B, sometimes referred to as Christmas disease[1], is a bleeding disorder caused by a deficiency of Factor IX, a soluble clotting factor. *"The biological roles of Factors 8 and 9 are closely related ... and so the clinical picture that is caused by these deficiencies is near identical"*: Expert Bleeding Disorders and Blood Disorders Report **[EXPG0000002 p19]**. Prior to 1952 patients were categorised under a generic diagnosis of haemophilia, but by 1952 it was possible to identify haemophilia B as separate from haemophilia A, using the thromboplastin generation test. Haemophilia B is, however, less common than haemophilia A: according to the Expert Bleeding Disorders and Blood Disorders Report, *"the National Haemophilia Database has 1,836 reported cases of haemophilia B of whom 360 are severe, compared to 8,410 cases of haemophilia A of whom 2,060 are severe"*.

[1] According to an article by Dr Rosemary Biggs and others – *Christmas Disease: A condition previously mistaken for haemophilia* BMJ, Dec 27 1952, 1378 – the condition was to be called "Christmas disease" after the name of the first patient examined in detail. [**HSOC0022584**]

4. As with haemophilia A, haemophilia B can be classed as severe (<1% factor IX), moderate (levels of 1-5%) and mild (>5%).

5. Prior to the availability of Factor IX concentrates, treatment of haemophilia B was with fresh frozen plasma (FFP). Tranexamic acid can be used in the treatment of haemophilia B. Desmopressin (DDAVP) is not an effective treatment for haemophilia B.

Production and use of Factor IX concentrates

6. An overview of the use of Factor IX products between 1960 and 1985 was given by Dr Charles Rizza in his report for the HIV litigation **[HCDO0000394 p34]**:

> "*Throughout the 1960s supplies of NHS Factor IX were limited and were reserved mainly for patients undergoing surgery. From 1969 onwards there was a slow increase in the availability and use of NHS Factor IX from approximately 0.5M units in 1969 to 18M in 1988. The UK has been self sufficient in Factor IX since about 1970 and there has been little usage of commercial Factor IX except for a short period in 1985 when some Directors of Haemophilia Centres purchased commercial Factor IX in preference to NHS Factor IX because the commercial material had undergone heat treatment.*"

7. Factor IX concentrates were first used in the UK in 1960. They were prepared by Dr Rosemary Biggs, Dr Ethel Bidwell and colleagues at the Blood Coagulation Research Unit[2] in Oxford using residual material derived from the plasma fractionation process of BPL. In an article entitled *"The Preparation and Assay of a Christmas-Factor (Factor IX) Concentrate and its Use in the Treatment of Two Patients"* published in 1961 in the British Journal of Haematology, Dr Biggs and colleagues described the

[2] The Blood Coagulation Research Unit was headed by Dr Macfarlane. The Unit closed in 1967, but the work conducted there provided a foundation for the establishment of the Oxford Haemophilia Centre (OHC). Dr Biggs served as the Director of the newly opened OHC until her retirement in 1977, when Dr Rizza took over. The Protein Fractionation Laboratory (PFL) was established within the OHC building in 1968. Dr Ethel Bidwell was the Head of Laboratory at PFL until her retirement in 1981, and was personally responsible for developing therapeutic concentrates of human factor IX concentrates for the treatment of haemophilia B **[WITN3431001 p19 para 50]**.

advantages of preparing intermediate (purity) Factor IX concentrates using this process **[RLIT0000043_018 p15]**:

> "*Whole blood is clearly a very extravagant starting material for the preparation of Christmas factor since many other useful components are discarded. Using the residue of a large-scale fractionation, there is no waste as all of the other useful components are preserved. It seems probable that a process such as we have described would be applicable to the appropriate fraction of the Cohn procedure. The integration of the preparation of Christmas factor into the large-scale fractionation procedures clearly opens up the possibility of a reasonable supply of the factor for general use.*
>
> *The material we have used contains large amounts of prothrombin and probably also of Factors VII and X, although we have made no specific tests for these factors. Patients with liver disease are commonly deficient in Factors VII and X and prothrombin, and such deficiencies occur congenitally. The material we have used produced a very marked rise in prothrombin and might very well be an ideal preparation for the treatment of patients with liver disease who require operation, and for haemorrhage in the congenitally deficient patients.*"

8. The early treatment, using Factor IX concentrate, of patients with haemophilia B at Oxford is described in the Wellcome Seminar *Haemophilia: Recent History of Clinical Management* [**RLIT0000022 pp. 19, 22, 28**].

9. Several intermediate Factor IX products were subsequently licensed in the UK during mid-late 1970s, including Baxter's/Hyland's 'Proplex Factor IX Complex' (licence PL 0116/0049 granted on 15 October 1976) **[MHRA0033316_007, MHRA0033317_054, MHRA0033317_067]**, BPL/PFL's 'dried human Factor IX Fraction' (licence PL 0134/0009 granted on 3 February 1977) **[CBLA0000569]** and PFC's 'Human Factor IX Concentrate DEFIX' (licence PL 3473/0008 granted on 16 July 1979) **[SBTS0004085_029]**. See further the Inquiry's Overview Chronology of the Licensing of Commercial Blood Products **[INQY0000411, INQY0000412]**.

10. BPL's application included, in the product particulars, a statement that *"Administration may be accompanied by a risk of transmitting serum hepatitis"* **[BPLL0006327_002**

p3]. The sample labels included the statement *"Less than 5000 plasma donations used in the preparation of this batch"* **[BPLL0006327_002 p7]**.[3]

11. As availability of NHS Factor IX increased, its regular administration became a possibility. At the meeting of haemophilia centre directors on 5 April 1971, Dr Bidwell described the preparation of Factor IX and asked how much was likely to be needed in England and Wales. It was reported, in the context of a discussion about the desirability of using Factor IX for patients other than those with Christmas disease, that at present the material was only sent to Directors of Haemophilia Centres **[HCDO0001014 p7]**. There was a general feeling among Haemophilia Centre Directors "*that regular administration of factor IX to severely affected Christmas disease patients was beneficial"*. Regimes of *"weekly, fortnightly or even monthly administration had been tried with success"* and such treatment *"was to be recommended for the very severely affected Christmas disease patient whenever this was possible*" **[HCDO0001014 p11]**. A witness to the Inquiry who received Factor IX treatment in the mid-1970s recalls that at the time "*there was a massive push for people to go on to home treatment*" **[WITN1105001 p2 para.5]**.

12. At the 27 October 1972 meeting of Haemophilia Centre Directors **[HCDO0001015 p11]** Dr Bidwell explained that she had asked directors to tell her how much material they would need to treat all their Christmas disease patients with concentrate instead of plasma *"and from the replies she estimated that she could meet the annual demands from the Directors to keep the patients treated at the present level of treatment"*. It was noted that she had also asked directors to forecast what their needs would be in the future *"and there were wide differences in the estimates from Centre to Centre"*. Dr Bidwell *"was looking into this further"*.[4]

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[3] In early March 1976 Dr Bidwell wrote to Dr Maycock, explaining that she would *"like to put our pool size for factor IX to the maximum consistent with one batch on our freeze drier (some 360 bottles) i.e. approx. 500l of plasma which would be higher than your present intention for factor VIII"* **[CBLA0000341]**. In his response of 19 March 1976, Dr Maycock agreed *"on the understanding that the final pool is prepared from 2 or 3 subpools (eluates) each of which has passed its safety tests, including RIA test for the presence of HB_sAG"* **[CBLA0000346]**.

[4] The minutes also record (at p. 14) a short discussion about laboratory precautions to be taken to protect staff against infection with hepatitis.

13. In an article entitled *"Haemophilia Treatment in the United Kingdom from 1969 to 1974"* published in 1977 in the British Journal of Haematology **[PRSE0004645]**, Dr Biggs reported that plasma and NHS Factor IX were the therapeutic materials used for haemophilia B, and that there was an increase in the average amount of Factor IX units used per patient over time. Dr Biggs predicted an increase in the demand for Factor IX resulting from the prolonged life expectancy of haemophilia B patients, and noted further uncertainty on demand due to the increasing use of Factor IX for the treatment of conditions other than haemophilia B. A table recording the total number of patients attending for treatment at the centres participating in the 1969-1974 survey gave a figure of 388 people with haemophilia B.[5]

14. Discussions at subsequent meetings of the United Kingdom Haemophilia Centre Directors provide further information about the production of Factor IX and its use in the treatment of people with haemophilia B.

    a. At the meeting on 13 January 1977 Dr Bidwell reported that in 1972, as a result of a questionnaire to the directors, she had estimated the Factor IX requirements to be about 5,000 bottles a year and had arranged to be able to make 7,500 bottles a year. By 1976 in fact nearly 10,000 bottles were used. In 1976 she had asked those directors whose requirements had increased considerably if they had changed their policy, explaining that *"present arrangements for production of factor IX and level of funding did not allow for prophylactic treatment except for occasional short periods of time."* She had since discovered that a few very severely affected patients were in fact on prophylaxis in Oxford and she thus *"felt that she should inform Directors that prophylaxis for severely affected patients may not be excluded if it were shown not to result in substantial increased usage."* Dr Rizza explained that 13 severely affected Christmas disease patients at the Oxford Centre had been put onto home treatment and regular prophylactic doses of Factor IX concentrate, having received prophylactic treatment (one bottle of concentrate every fortnight or every week,

[5] The same article includes (at pp.11-12) a discussion about the occurrence of hepatitis in patients treated for haemophilia A and B. After a short discussion about hepatitis B, the article notes that *"Many patients who develop jaundice do not develop hepatitis B surface antigen or antibody in their blood and it is to be presumed that the have been infected by some other virus or have developed jaundice from some other cause"*.

depending on the size of the patient) at the Centre before commencing home treatment. He suggested that the treatment was very effective and the patients did not use much more material than for *"on demand"* treatment" **[PRSE0002268 p22-23]**.

b. At the meeting on 24 October 1977 Dr Bidwell observed that the amount of Factor IX concentrates being issued from the PFL at Oxford was still rising but was showing signs of levelling off. She reminded directors that the product was licensed for use only in patients with congenital deficiencies of Factor II, IX and X and that its use in other deficiency states required *"a prescription for a named patient, and also a detailed report of the circumstances in which it was used, and its effect."* **[PRSE0001002 p15]**.

c. At the meeting on 13 November 1978, Dr Bidwell reported that she had asked directors to let her know their estimated requirements for 1978 onwards and those estimates already showed a 20% increase over the previous year. She stressed the importance of having accurate estimates since considerable capital investment on freeze drying and other equipment would be needed at the PFL if the demand for Factor IX concentrate continued to increase. Dr Bidwell noted that several directors had explained that they were treating small children who were growing and therefore requiring more treatment *"but in general there was no clear-cut reason for the increase in usage"* **[HSOC0010549 p18]**.

d. A meeting of Haemophilia Reference Centre Directors on 15 October 1979 **[PRSE0000539]** considered a report from the Home Treatment Working Party, which recorded that home therapy figures for 1978 showed that 87 haemophilia B patients were on home therapy **[LOTH0000012_135].**[6]

e. At the Haemophilia Centre Directors' meeting on 20 November 1979 Dr Rizza presented a report on the 1978 annual returns, which were said to indicate that there was a decrease in the amount of Factor IX used to treat Christmas disease patients. Dr Bidwell stated that she had calculated the amount of Factor IX for 1979 on the basis of the usage during the first ten months of the year; this indicated that there was likely to be a decrease in the amount of Factor IX used

[6] The same report showed that 719 haemophilia A patients were receiving home therapy.

during 1979, compared with 1978 **[CBLA0001028 p6-7]**. Dr Bidwell invited directors to make requests before 39 November for Factor IX supplies sufficient to cover anticipated needs to mid-January **[p17]**.

f. At the Directors' meeting on 30 September 1980 **[PRSE0003946 p8]** the PFL was congratulated on the good quality and adequate amounts of Factor IX concentrates which were produced.

g. At the meeting of Haemophilia Reference Centre Directors on 23 February 1981 **[HCDO0000407]** Dr Kernoff reported that a hepatitis-free Factor IX concentrate was now available in Germany. It appears to have caused a degree of uneasiness: Dr Kernoff felt that if they were marketed in the UK clinicians would "*find themselves in the difficult position of having to decide whether or not to give this material to all patients or to restrict its use to certain categories of patients*" **[HCDO0000407 p10]**.

h. A study was undertaken at Oxford[7] – Project Number J/S240/78/7 – on the epidemiology and chronic sequelae of Factor VIII and Factor IX associated hepatitis in the UK. The second annual report on this study **[OXUH0001874]** explained that, in addition to the follow up of 148 patients on Oxford receiving long term Factor VIII, haemophilia B patients on NHS Factor IX therapy had also been assessed. A table in Appendix II to the report **[p41]** provided details of changes in liver function tests in Oxford patients on regular treatment with Factor IX concentrate in 1980: of 16 patients, 5 had a persistently abnormal AST level (between 35 and 70 i.u./1) and 2 had a persistently abnormal AST level of more than 70 i.u./l.

i. The minutes of the meeting on 9 October 1981 **[DHSC0001312 p13]** record that there had been a slight increase in the amount of Factor IX used and in the number of Christmas disease patients treated. There was a discussion about the claims from commercial firms that there was now available a hepatitis-free Factor IX concentrate: *"Dr Craske thought that this may well be true but there were problems in proving the safety of each batch of concentrate made as only*

[7] Involving Dr Craske, Dr Rizza, Miss Spooner, Dr Ghosh, Dr Trowell, Dr Ludlam and Dr Lane: **OXUH0001874 p4.**

a limited number of laboratory animals were available for testing the materials" **[p21]**.

j. At the meeting on 13 September 1982, during a discussion about the annual returns for 1981, the minutes recorded the following: "*With reference to the use of commercial factor IX concentrates, Dr Snape of the Plasma Fractionation Laboratory pointed out that the P.F.L. was able to meet all demands made to them for supplies of factor IX concentrate. No request for factor IX had been turned down, therefore the use of commercial factor IX did not mean that the NHS was unable to meet its demands for NHS factor IX concentrate*" **[CBLA0001619 p5]**.

Scotland

15. In relation to Scotland, a report - produced by Professor Cash for the purposes of a January 1981 meeting between haemophilia centre directors and regional transfusion directors in Scotland **[PRSE0000144]** – recorded that because of the much smaller number of haemophilia B patients, the supply of Factor IX concentrates from the PFC was "*always more than adequate*". It appears that the amount of PFC Factor IX DEFIX supplied doubled from 500,000 i.u. in 1975 to 1,000,000 i.u. in 1980 **[CBLA0001252 p11]**. The report continued: *"Several reports have implied that the risks of transmitting agents likely to cause hepatitis is higher for factor IX than VIII concentrates. The evidence is not firm but may relate to differences in pool size (the former usually being larger). Nevertheless, continuing efforts are being made to improve matters and a stage has been reached at P.F.C. when clinical studies will soon be required."* Haemophilia B patients were described as *"a high risk group for hepatitis"*.

16. The report also recorded that a new Factor IX product – Supernine - was at an advanced stage of development: *"Further purification of DEFIX has led to a product which we believe may be both safer with regard to virus transmission and thrombogenicity"*.

17. The Scottish Haemophilia and Blood Transfusion Working Group discussed, at its meeting on 4 March 1981 **[SBTS0000382_008]**, the setting up of clinical studies of Supernine. The West and South East Regions were reported to have access to a limited amount of Supernine and a licence had been given for clinical trials. The *"main aim*

was to obtain a product licence". A discussion also took place about ways of determining quantities of Factor IX concentrates used in haemophilia B and non-haemophilia B patients on an annual basis, Professor Cash expressing concern about the inadequate tracing of patients and lack of available data. It was agreed that *"there should be an effective method of monitoring blood products, recording what product is given to a patient and how the products are used"*.

18. The minutes of the meeting of SNBTS directors and haemophilia directors on 21 January 1983 **[PRSE0001736]** reported that the supply position of DEFIX over the last 5 years *"had remained strong and the demand reasonably stable"*. The clinical studies on Supernine *"had produced excellent results"* and it was not thought necessary to obtain a separate product licence, as a variation of the DEFIX licence on a named patient basis was considered sufficient. It was also reported that studies of heat treatment, to reduce hepatitis risk, were currently under way using Supernine, but the rate of progress would be slower than with Factor VIII because of the need to submit the heated IX concentrate to intensive animal studies to assess thrombogenicity.

Treloar's

19. Letters from 1975 show that the Lord Mayor Treloar College was aware of increased incidence of jaundice among boys with haemophilia B **[HHFT0000930; TREL0000169_033]**. In a letter addressed to a consultant paediatrician at the Great Ormond Street Hospital for Sick Children, Dr Rainsford remarked that "*we have always assumed that this is due to the fact that the Christmas boys are almost invariably transfused with high potency factor IX prepared with material from large donor pools. However, I think this is a debt we shall have to continue to pay, since this high potency concentrate is so effective and no case of hepatitis that we have experienced can be regarded as even moderately severe*" **[TREL0000169_033]**.

Treatment advice in response to risk of AIDS

20. The minutes of the special meeting of Haemophilia Reference Centre Directors on 13 May 1983 **[HCDO0000003_008]** contain no reference to the use of Factor IX

concentrates or the treatment of patients with haemophilia B. However, the recommendations subsequently circulated on 24 June 1983 by Professor Bloom and Dr Rizza **[HCDO0000270_004]** referred to two matters having been drawn to their attention since the 13 May meeting: *"The first concerns the treatment of patients with haemophilia B. The evidence to incriminate factor IX concentrates in AIDS is even less than with factor VIII and it seems logical to continue to use our normal supplies of NHS concentrate."*

21. No further advice was issued by UKHCDO until the production of the AIDS Advisory Document **[HCDO0000270_007]**, following the meeting at Elstree on 10 December 1984 **[HCDO0000394_117]**[8]. The AIDS Advisory Document recorded that various commercial heat treated Factor IX concentrates were available:

> "*Profilnine (heated) (Alpha), heated Konyne (Cutter) and Immuno (heated Prothromplex) are available at prices up to 20p a unit but the effects on efficacy and thrombogenicity are unpublished. Since AIDS and laboratory changes seem (controversially) to be less common in Christmas disease than haemophilia A no firm recommendation can be given on heated factor IX.*
>
> *Heated Feiba is also available from Immuno at 30p a unit but is probably not cost-effective.*"

The following treatments for haemophilia B were recommended (emphasis in original):

> "*(a) <u>Mild Christmas</u> Fresh Frozen plasma if possible (otherwise NHS Factor IX.*
>
> *(b) "Virgin" Patients and those <u>not previously exposed to concentrate</u> use fresh frozen plasma (or NHS factor IX concentrate if essential)*
>
> *(c) <u>Severe</u> and <u>Moderate Christmas Disease previously exposed to factor IX concentrate</u> continue to use NHS factor IX.*"

22. It was further generally advised that *"In individual patients there may need to be a choice. In general heated concentrate appears to be the recommendation of virologists*

[8] The meeting on 10 December 1984 appears to have focused primarily on the use of Factor VIII. The note taken by Mr Pettet of BPL recorded that: *"Some discussion took place on the use of Factor IX. It was felt that the main problem was in balancing the risk of HTLV III against the risk of increased thrombogenicity associated with HT – Factor IX."*

consulted but individual Directors may wish to make up their own minds. This is particularly true of unheated NHS material."

23. Some clinicians began to switch from unheated NHS Factor IX to commercial heat-treated Factor IX for the treatment of haemophilia B. The AIDS Group of Haemophilia Centre Directors held their first meeting on 11 January 1985, and the minutes of that meeting record that there was *"some difference of opinion with regard to factor IX. Some Centres had stopped using NHS factor IX and were now using heated commercial factor IX while others intended to continue for the meantime with the unheated NHS factor IX*" **[HCDO0000521 p4]**. By the time the AIDS Group held its 5th meeting on 17 June 1985, it was reported that most Reference Centres had transitioned to using commercial heat-treated Factor IX, and at this meeting the Group agreed that a recommendation should be made to Haemophilia Centre Directors to use only heat-treated products **[HCDO0000523 p4]**. The annual returns data which the Inquiry has examined confirm that (heated) commercial Factor IX concentrates began to be used (on a named patient basis) in centres in the course of 1985, but that centres also continued to use (unheated) NHS Factor IX.[9]

24. It was not until October 1985 that all Factor IX issued by BPL had undergone heat treatment. Dr Snape explained the timing in his Inquiry statement as follows **[WITN3431001 p69 para 191]**:

> "*BPL was more cautious in the evaluation of heat treatment on our Factor IX concentrate (the unheated concentrate was coded "9D", the heated product "9A"). Although the programme of work began at the end of 1982, the heated product 9A was only released for clinical trial in selected centres in July 1985, three months after the first trial batches of 8Y. We were especially concerned to rule out the potential for thromboembolic sequelae that might be caused by activated factors produced on heat treatment of the 9D product. Prothrombin complex concentrates in general had a history of association with problems of this sort and we were concerned that the risk might be increased by heating the concentrate.*"[10]

He confirmed that heated Factor IX (9A) was first issued by BPL in July 1985 (for a limited clinical trial of safety and efficacy only), and that all Factor IX issued after 2 October 1985 was type 9A, subject to HT3 heat treatment conditions **[para 192]**. Dr

[9] See also **WITN3826017**.
[10] See also **WITN3433001** – the statement of Dr James Smith – at paras 71-73.

Snape's understanding **[para 193]** was that during the first 9 months of 1985 most treatment centres continued to use the BPL unheated product, although heat treated US Factor IX products were available.

25. According to the National Haemophilia Database/UKHCDO report *Bleeding Disorders Statistics for the Infected Blood Inquiry 2022*, 18 people with severe haemophilia B were infected with HIV **[WITN3826016 p40]**. In relation to people with non-severe haemophilia, the table does not distinguish between haemophilia A and haemophilia B but simply provides an overall figure of 305 infected with HIV.

The experiences of people treated with Factor IX concentrates

26. The Inquiry has received and considered many statements from, or about, people with haemophilia B who were infected with HIV and/or HCV and/or HBV. This presentation note does not seek to set out or summarise all of this evidence. However, a common theme running through most such statements is the lack of information provided to people about the risks of treatment. Some examples are given below.

    a. An anonymous witness **[WITN0053001]** (mild haemophilia B) underwent an operation in 1984 to remove a birthmark, following which he received treatment with Factor IX concentrate. At no stage was any cautionary information given and in his statement he has questioned why, as a patient he was allowed to undergo an elective, non-vital procedure at a time when it was known that factor replacement therapy was potentially both HIV and HCV infectious.

    b. An anonymous witness **[WITN0369001]** (severe haemophilia B) was treated with Factor IX concentrates first in 1975 at St James Hospital, Leeds. He received treatment at Addenbrooke's Hospital between 1975 and 1978 and then in Edinburgh from 1978. He considered that he was given adequate information according to what was understood at the time by medical professionals, other than the fact that he was not told he had raised liver function tests and being told about abnormal test results if and when they were found was an important point for him.

c. Matthew Johnson **[WITN1057001]** (severe haemophilia B) was treated at the Oxford Haemophilia Centre. Between 1981 and 1983 he began to be treated prophylactically. His parents were assured that if he were to contract hepatitis it would be no more severe than a bad cold. They were not told the true risks. In his oral evidence to the Inquiry on 3 May 2019 **[INQY1000004, p.1]** Mr Johnson explained that his parents *"were told that this product was ground-breaking, it was clean and it was as good as good can be"*.

d. Jonathan Ainsworth **[WITN1069001]** (severe haemophilia B) was treated at Manchester Children's Hospital. Between 1981 and 1985 he was treated with BPL Factor IX. In February 1985, when he was around 5 years old, he was treated with a commercial Factor IX concentrate (Cutter). He was told by his mother that he had been treated with a US product on that occasion as there was a shortage of what he normally received.

e. Colin Catterall **[WITN1145001]** (moderate haemophilia B) was given Factor IX for the first time in 1978/9 at Lancaster Hospital for a tooth extraction. He was also treated with Factor IX at Preston Royal Infirmary. He was not given any information about FIX and risks; his father recalled only being told that it was a new treatment in the 1970s when it was first administered but he was not told anything more than that.

f. An anonymous witness **[WITN1149001]** had mild haemophilia B and his mother was a carrier of haemophilia B. Both were treated with Factor IX concentrates at Oxford Haemophilia Centre and infected with HCV. As far as the witness was aware his mother was not given any advice or information regarding the risks of receiving blood products.

g. An anonymous witness **[WITN1158001]** (severe haemophilia B) received home treatment and weekly treatment at school with Factor IX. He was infected with HIV between 1983 and 1984. No advice was given regarding the risks of treatment. He was told treatment was a step in the right direction and would give him a better quality of life. When invited to be tested by Manchester Royal Infirmary he was unaware that the test was for HIV. He was told by letter that

he had tested positive for antibodies and was not given any follow up consultation.

h. Barrie Dennis **[WITN1185001]** (mild/moderate haemophilia B) was treated with Factor IX from BPL on 7 occasions between 1977 and 1989, often for dental work. He was told that it was made up of blood plasma from hundreds of people but was not given any information about potential risks of treatment. Mr Dennis died in the summer of 2022.

i. An anonymous witness **[WITN1320001]** (severe haemophilia B) was treated at Birmingham Children's Hospital with Factor IX concentrates. His parents were never told about the risks of infection.

j. Trevor Marsden **[WITN1372001]** was treated with Factor IX concentrates from the mid-1970s, whilst under the care of the Belfast Haemophilia Centre. He told the Inquiry during his oral evidence on 9 October 2019 [**INQY1000038 p1**] that he was *"absolutely not"* given any warnings or advice or information about any risks of infection associated with Factor IX products.

k. John Morrissy **[WITN1409001]** (severe haemophilia B) received Factor IX at Manchester Children Hospital and at other hospitals. His parents were told that it was a wonder drug – nothing concerning was discussed nor any side effects.

l. Stephen Nicolls **[WITN1432001]** (severe haemophilia B) joined Treloar's in 1976. From when he was about 11 the school started to push prophylaxis and was *"very insistent"* about regular treatment. There was no mention of risks or dangers and no discussions as to the balance of benefit with his parents or with him. In his oral evidence to the Inquiry on 1 May 2019 **[INQY1000002, p.10]**, Mr Nicholls said this: *"There was a really, really big push in those years to get as many haemophiliacs as they could onto prophylactic treatment. Again, there was no risk assessment done to me. They didn't say this stuff contains a risk. Obviously the more you have, the greater the risk. That wasn't explained at all.*

It was just sold to you purely, 'This will give you a more normal life. You'll have more free time. You'll be fitter, so take it.'

m. Paul O'Hora **[WITN1440001]** (mild haemophilia B) was treated at Belfast Haemophilia Centre. He was certain that he was never informed at any time that there was a danger of picking up any disease from blood products.

n. Cain Squires **[WITN1538001]** (moderate/mild haemophilia B) was treated in Nottingham on a regular basis with Factor IX. He was given no advice regarding risks and believed that his mother was also given no such advice when he was a child.

o. David Whistler **[WITN1603001]** (moderate haemophilia B but fluctuating) was treated with Factor IX concentrates from the late 1970s/early 1980s (having previously been treated with plasma) at the Bristol Royal Hospital for Sick Children and Bristol Royal Infirmary. Neither he nor his mother were told that the treatment carried any risk of infection.

p. John Shackleton **[WITN1705001]** (severe haemophilia B) was treated at Blackburn Royal Infirmary with Factor IX concentrates. There was no discussion about any risks associated with FIX – his mother was informed that it was safe to use and would allow him to lead a "normal" life.

q. The husband of Susan Sparkes **[WITN1713001]**, Les, had moderate haemophilia B and was treated with Factor IX concentrates at Cardiff Haemophilia Centre. As far as she was aware, no information was provided to him about the possibility of being infected by the products. He was treated predominantly with 9D (the BPL/PFL product) but in July 1985 received Profilnine. There was no discussion about the change of product on that occasion: see the oral evidence of Mrs Sparkes on 23 July 2019 [**INQY1000033 p18**].

r. Carol Carruthers **[WITN1850001]** is the widow of Ollie Carruthers, who was a patient at the Royal Victoria Infirmary in Newcastle and who rarely had bleeds.

He was treated with prophylactic Factor IX when he had dental treatment in 1977 and 1978 and was never made aware of the risk of infection. In May 1989 he had a tooth extraction and was given Factor IX, despite having raised concerns about the need for, and safety of, such treatment; as Mrs Carruthers said in her oral evidence on 30 October 2019 [**INQY1000047 p12**] *"he trusted that the doctors wouldn't knowingly put him at risk"*.

s. An anonymous witness [**WITN1880001**] (very mild haemophilia B) was infected with HCV following treatment at the Royal Hallamshire Hospital with Factor IX in December 1979 following a tooth extraction. Neither he nor his father (who attended appointments with him) were told that there was a risk of infection.

t. Myles Hutchison [**WITN2168001**] (moderate haemophilia B) and Paul Hutchison [**WITN2167001**] (moderate/severe haemophilia B) gave oral evidence to the Inquiry on 31 October 2019. Myles confirmed [**INQY1000048 p11**] that no advice or information or warning was provided to their parents about any risk of information: *"They were assured all the time that it was perfectly safe"*. In response to the question whether any alternatives to twice weekly prophylactic treatment were discussed with their parents, Myles confirmed *"None whatsoever"*.

u. An anonymous witness **[WITN2212001]** (moderate haemophilia B) was treated at Yorkhill and Glasgow Royal Infirmary (and infected with both HIV and HCV). No advice was given to him or to his parents about risks of infection: *"The Factor 9 would just have been administered and that is what the hospital told you that you required as a treatment"*. At no point were any alternatives to treatment discussed.

v. Bruce Norval **[WITN2235001]** (moderate/severe haemophilia B) was treated with Factor IX concentrates (mostly from PFL, but also with commercial products). His parents *"were told that I might get a touch of hepatitis when I was young. They were told that it was mild and that I would clear it as haemophilia boys always recovered from it. It would be Dr Howard Davies at*

the Royal Infirmary that told my parents that at the time. My parents were not formally told there was a risk of infection from the products I was receiving. They were told that there was a possibility. It was worded in a very non-risk fashion. It wasn't highlighted and it was very much played down."

w. An anonymous witness **[WITN2294001]** (severe haemophilia B) recalled being told in the 1970s by Dr Forbes at Glasgow Royal Infirmary that there was a new treatment – Factor IX concentrate. In response to a question about whether there were any risks Dr Forbes said *"Not really"*. He said that there was a risk of a type of hepatitis, but not to be alarmed, it was not the type read about in the papers and the effects *"would be the equivalent of a stomach upset"*.

x. Nigel Miller **[WITN2510001]** (severe haemophilia B) was treated with FFP until 1977 when he began to received Factor IX. Home treatment began in 1979. He was treated at Royal Devon & Exeter Hospital. In 1985 and 1986 he was given Profilnine at St James University Hospital Leeds. There was no discussion about it being a different product.

y. Gerald Stone **[WITN2554001]** (severe haemophilia B) was treated with Factor IX (British) from about 1970/71, initially in Oxford and then in Cardiff. From about January 1976 he was on home treatment. In his oral evidence to the Inquiry on 23 July 2019 **[INQY1000033 at p8]** he confirmed that he was not told anything at the time about the risks of infection. He was aware at some stage of the possibility of hepatitis B but was not unduly worried about it because there was a vaccination for it. Between October and December 1985 he was given US products and was told by Professor Bloom that the US products were safer than the British ones. Mr Stone set out in his oral evidence his understanding that he was infected with HCV as a result of the particular batch of Profilnine he received (which was also used to treat Mr Miller, above – see Mr Stone's oral evidence at p.11).

z. Cressida Haughton **[WITN3125001]** provided a statement regarding the treatment of her late father, who received Factor IX as an inpatient in 1966 recorded as a *"new method of fractionation for testing"*; she noted that *"I don't*

think my father was aware he was being given experimental FIX, as I believe he would have written it down in his book if it was with his consent".

aa. An anonymous witness **[WITN3160001]** (female with mild haemophilia B) was first given Factor IX concentrate in 1980 for dental treatment at Royal Stoke Hospital. She did not know she was being given a blood product, she was not told what it was and she was not told about any risks of infection. She had a second treatment with Factor IX concentrates in 1987. On that occasion she had said she did not want to receive Factor IX because of the fear of HIV but she was given it whilst drowsy from pre-med and felt that she was not given a real choice.

bb. An anonymous witness **[WITN3193001]** (severe haemophilia B) was treated at St James Hospital under Dr Swinburne. He was first treated with FFP in 1966 and recalled that this was a better treatment than whole blood which he had previously had. If he had a bleed, he would go to hospital at the end of the day, be treated overnight and then go back to work in the morning. He began to be treated with Factor IX concentrates in the early 1970s. He was a young adult at that time and was not informed about the risks of blood borne infections. He was told that the product was new and exciting and recalled that it was referred to as *"Jungle Juice"* by Dr Swinburne. Home treatment began in 1983. He was treated with exclusively domestic Factor IX until June 1985 when he had his first treatment with Profilnine. He was not advised that the product had changed or of the reasons for the change.

cc. An anonymous witness **[WITN3245001]** (mild haemophilia B) was treated at Oxford Haemophilia Centre and given Factor IX concentrate once or twice in 1976/77 when having dental treatment. His parents were not informed of any risks of infection.

dd. Elizabeth Hooper's **[WITN3514001]** first husband, Jeremy Foyle, had severe haemophilia B. He was treated with Factor IX concentrates at the Oxford Haemophilia Centre: *"No advice was provided to Jeremy (or his parents) about the risk of being exposed to infection from FIX. It was hailed as a wonder drug."*

ee. An anonymous witness **[WITN3854001]** whose son had haemophilia B recalled becoming aware that there was a problem in the late 1970s in relation to blood products *"but the nature of the problem was not fully explained"*. His son did not receive heat treated material until about December 1985. He did *"not believe that adequate information was provided to us when it should have been. The doctors failed to give us the full extent of the nature of the risk. As stated above we recognised some sort of risk."*

ff. The mother of an anonymous witness **[WITN3975001]** had mild haemophilia B and was treated at Leicester Royal Infirmary with Factor IX concentrates. The witness did not believe their mother was given any warnings about risks: *"She thought the FIX concentrate safe to use."*

gg. The son of Patricia Carrington-Howell **[WITN5237001]** had mild haemophilia B. He was under the care of Dr Strevens at Coventry and Warwickshire Haemophilia Centre. He was treated with Factor IX concentrate on two occasions – for an operation on the foot in 1983/4 and for tooth extraction in 1986/7. They were not warned of any risks before he had the treatment.

hh. Irene Brierley **[WITN5520001]** provided a statement regarding the treatment of her husband Brian (severe haemophilia B). He was first treated with Factor IX concentrates in the second half of the 1970s. No one warned them of the risk of infection and they were *"so impressed with the new FIX treatment. It was the best thing ever"*. Later Brian began to worry about the Factor IX concentrate through articles he was reading. He asked several times if it was heat treated and was told that it was. In early 1985 he was specifically told, by the nurse under instruction from Dr McVerry (Liverpool Royal Infirmary) that the Factor IX was from the UK, was heat treated and was safe to inject without fear of infection. Some months later Brian was informed by letter that he was HIV positive.

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