# Infected Blood Inquiry

## Presentation by Counsel to the Inquiry

## Self Sufficiency: Pool Sizes at the Blood Products Laboratory

1. Introduction
2. Pool sizes at the Blood Products Laboratory
3. Decisions to increase pool sizes at the Blood Products Laboratory
4. Conclusion

## Section 1: Introduction

Structure of the presentation

1. This is a presentation by Counsel to the Inquiry on the pool sizes used to manufacture factor concentrates (Factor VIII and Factor IX) at the Blood Products Laboratory ("BPL") in the 1970s and 1980s. The focus of this presentation is on:

    a. the size of the pools used to manufacture factor concentrates at BPL and the extent to which pool sizes increased **(Section 2)**; and
    b. the reasons underlying decisions to increase pool sizes **(Section 3)**.

2. This presentation should be read alongside the Chronological Presentation on Domestic Production and Self-Sufficiency in England and Wales and its appendices ("the Chronological Presentation"). The same caveats apply. In particular this should not be seen as a comprehensive history but an overview of some of the more significant events. Efforts have been made to avoid repetition with the previous presentations, particularly in respect of "small pool" and "small panel" fractionation at PFL in the 1980s. The presentation is intended as a neutral, factual narrative. All Core Participants will have an opportunity to make submissions on pool sizes, and the Chair's findings will be informed by all such submissions.

Sources and references

3. This presentation draws on a range of documents that have been disclosed to and by the Inquiry. Although voluminous, the documents are by no means comprehensive. As is to be expected at a distance of 40-50 years, archives are incomplete and difficult to navigate. The Inquiry legal team have found

relatively few documents that record or communicate discussions and decisions around pool sizes at BPL and PFL. Few, if any, documents can be said to amount to a formal BPL policy as to pool size.

4. The citations to documents in this presentation use the Inquiry's referencing system. References to "[ep.]" are to the electronic page numbers of those documents, which are used in preference to the internal page numbers.

Definition of terms

5. The term *"blood product"* refers to any therapeutic product derived from human blood donations, including factor concentrates and cryoprecipitate.

6. The term *"pool"* refers to any mixture of blood components derived from multiple blood donations.

7. Unless otherwise stated, *"pool size"* refers to the number of blood donations in the pool, not to the volume or weight of the pool in litres or kilograms. In his written statement to the Inquiry, Dr T. J. Snape explained that *"donor pool size" [is] sometimes expressed as plasma pool size in litres or kg of plasma, but more usefully expressed as the number of individual donations included in the plasma starting pool"* **[WITN3431001, ep.75, para.212]**.

8. It should be noted that some documents express pool size in litres or kilograms. Where this occurs, it has been necessary to calculate the equivalent number of donations in the pool, so as to be able to compare different pool sizes **(Section 2)**, or compare the risks of smaller and larger pools **(Section 3)**. Where the number of donations in a pool has been calculated:

    a. the original figure, in litres or kilograms is in plain text; and

b. the number of donations is *(italicised in brackets)*.

The arithmetical basis on which the number of donations is calculated is discussed in **Section 2**.

## Section 2:

## Pool sizes at the Blood Products Laboratory

9. This section examines the size of the pools used to manufacture factor concentrates at BPL, and the extent to which pool sizes increased throughout the 1970s and 1980s.

Maximum limits on pool size

10. Two sets of documents provide evidence of the maximum limit on BPL pool size at a given time:

    a. BPL product labels; and
    b. Correspondence between BPL staff and staff at the Protein Fractionation Centre ("PFL") in Oxford.[1]

11. The product labels provide primary evidence of the maximum pool sizes permitted at BPL. They are examined first for this reason. Data on the maximum limits, as shown on product labels, are compiled in **Table 1** below.

12. **Table 1**: Maximum limits on BPL pool sizes as shown on product labels:

| Date and Product | Maximum pool size | Unique ID(s) |
|---|---|---|
| March 1976<br>Factor VIII | 1,500 donations | **CBLA0009269; CBLA0000046_017** |
| 19 August 1976 | 1,500 donations | **BPLL0004430_001** |

[1] **CBLA0000253; CBLA0000325; CBLA0000341; CBLA0000346; CBLA0001157; CBLA0001173; CBLA0001192; CBLA0001533; CBLA0002190; DHSC0002303_027; CBLA0004791**

| | | |
|---|---|---|
| Factor VIII | | |
| 21 September 1976<br>Factor VIII | 1,500 donations | **BPLL0004429_001;**<br>**CBLA0009762** |
| 11 September 1980<br>Factor VIII | 5,000 donations | **BPLL0001692_008** |
| 7 January 1983<br>Factor VIII (HL) | 7,500 donations | **BPLL0001692_009** |
| 11 February 1983<br>Factor VIII (8CRV)[2] | 7,500 donations | **BPLL0010430_001** |
| 12 March 1985<br>Heat treated 8Y | 10,000 donations | **BPLL0001692_009** |
| "Pre-June 1985"<br>Factor VIII | 7,500 donations | **BPLL0002039** |
| "June 1985 to<br>February 1987"<br>Heat treated 8Y | 10,000 donations | **BPLL0002039;**<br>**CBLA0002201** |
| "February 1987<br>onward"<br>Heat treated 8Y | No stated limit | **BPLL0002039** |
| 30 June 1988<br>Heat treated 8Y | No stated limit | **BPLL0016009_161** |
| Undated<br>Heat treated 8Y | No stated limit | **JPAC0000197_025** |

[2] 8CRV was a Factor VIII product produced at PFL rather than BPL. This label is included in this table as a point of comparison.

13. As seen from **Table 1**, the maximum pool sizes permitted at BPL increased significantly - by over 600% - from 1,500 donations in 1976[3] to 10,000 donations in mid-1985.[4] Thereafter, by at least June 1988 (and possibly as early as February 1987), the practice of specifying the maximum limit on BPL Factor VIII labels had been discontinued.[5]

14. Correspondence between staff at BPL and PFL also provides an indication of the maximum pool sizes permitted at BPL. This correspondence is useful because it shows what the maximum limits were after the practice of printing the limit on product labels ceased.

15. Unfortunately, it is difficult to extract reliable data from the BPL/PFL correspondence. The documents are sometimes unclear as to whether the stated limit applied to BPL, PFL or both facilities. The period in which a limit operated is also sometimes unclear. Therefore, data is only included in **Table 2** where the correspondence is clear as to the facility (BPL or PFL) and time-period involved. Data derived from BPL/PFL correspondence are shown in **Table 2** below.

16. **Table 2**: References to maximum limits on BPL pool sizes, BPL/PFL correspondence

| Date | Maximum pool size | Unique ID |
|---|---|---|
| 27 October 1980 | 5,000 donations | **CBLA0001192** |
| 25 January 1982 | 7,500 donations | **CBLA0001533; BPLL0002070** |
| 10 June 1985 | 10,000 donations | **CBLA0002190** |
| 20 June 1986 | 25,000 donations | **CBLA0004791** |

[3] **CBLA0009269; CBLA0000046_017**
[4] **BPLL0002039; CBLA0002201**
[5] **BPLL0016009_161; BPLL0002039**

17. In addition to showing the maximum pool sizes permitted at BPL, the BPL/PFL correspondence also illustrates why increases in BPL pool sizes occurred. This is examined fully in **Section 3**. A brief summary of the correspondence, including the reasons why some data was not included in **Table 2**, is set out below.

18. On 22 January 1975, Dr Bidwell wrote to Dr Maycock about product labels for BPL concentrates. The letter suggests that there had been an agreement to move from a position of putting the precise number of donations that went into each bottle to a generic label stating that the Factor VIII concentrate was produced from *"not more than 500 donations"* **[CBLA0000253]**. The Inquiry legal team has been unable to find any further documentation relating to Dr Bidwell's minute, and hence the figure has not been included in **Table 2**.

19. On 3 December 1975, Dr Bidwell wrote to Dr Maycock, stating that the limit on Factor VIII and Factor IX pool sizes at that time was 1,000 donations **[CBLA0000325]**, though she considered that it should increase in light of Dr Gunson's proposed policy of taking only 180ml of plasma from donations in Oxford. This figure is not included in **Table 2** as it appears to relate to PFL, not BPL.

20. On 2 September 1980, Dr J. K. Smith wrote to Dr Lane, requesting the maximum limit be increased to 900kg[6] **[CBLA0001157]**. On 29 September, Dr. Lane approved the increase **[CBLA0001173]**. This data is not included in **Table 2** because it appears to relate to PFL rather than BPL. (Dr Lane's comments in his minute of 29 September 1980 are discussed further below.)

21. On 27 October 1980, Dr Bidwell wrote to Dr Maycock to confirm that the PFL labels would show an increased limit of 5,000 donations, "*thus bringing it into*

[6] *(approx. 4,995 donations)*

*conformity with the BPL label* **[CBLA0001192]**. As the 5,000 donation limit explicitly applies to BPL, it is included in **Table 2**.

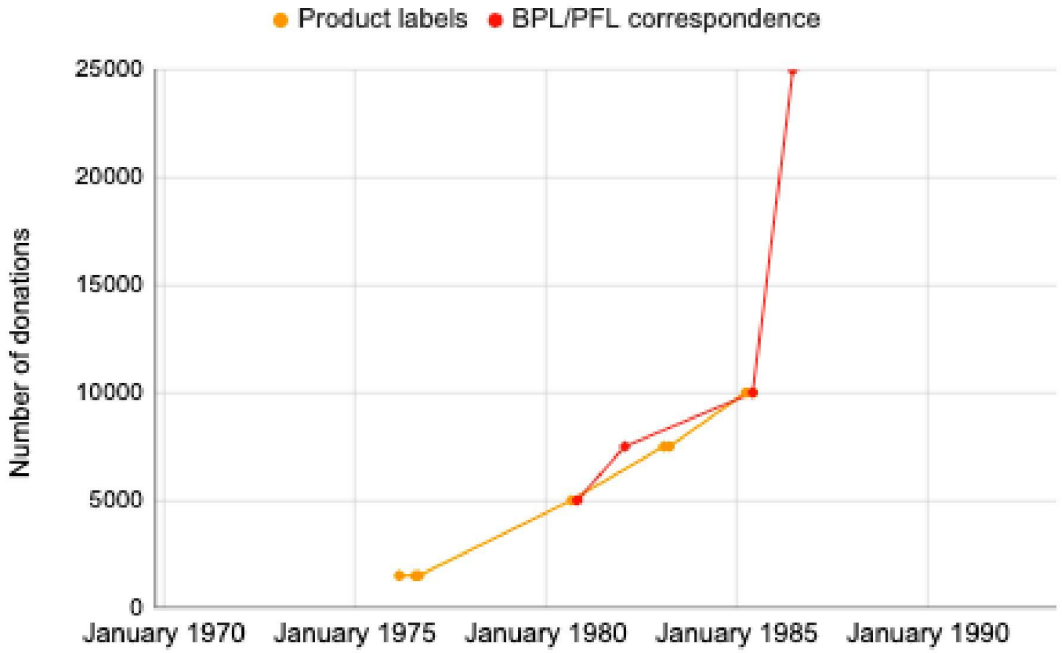
22. On 13 January 1982, Dr Smith wrote to Dr Lane asking that the maximum limit for Factor VIII and IX be increased to: "*1,200 kg, or 7,500 donations*" **[CBLA0001533]**. On 25 January, Dr Lane approved the increase **[BPLL0002070]**. It would appear Dr Smith's request was made in respect of both PFL and BPL because both "*PFL and BPL labels*" were to be adjusted **[CBLA0001533]**. This data is included in **Table 2**.

23. On 10 June 1985, Dr Snape stated that a limit of 10,000 donations would not restrict operations in the current BPL **[CBLA0002190]**. This data is included in **Table 2**.

24. On 20 June 1986, Dr T. J. Snape wrote to Dr A. Smithies (DHSS), advising her of a proposed increase in the maximum pool limit from 10,000 to 25,000 donations **[DHSC0002303_027]**. On the same day, Dr Snape wrote to Dr J. K. Smith and others, stating that Dr Lane had agreed to increase the maximum pool sizes to 25,000 donations for heat-treated factor concentrates **[CBLA0004791]**. This data is included in **Table 2**.

25. Data on the maximum limits of BPL pool sizes derived from product labels **(Table 1)** and BPL/PFL correspondence **(Table 2)** is presented in Figure 1 below.

26. **Figure 1**: Maximum limits on BPL pool sizes




Pool sizes: BPL Factor VIII: Dr Snape's estimates of 1989-1990

27. During the HIV Haemophilia Litigation, Dr Lane requested from Dr Snape information on the pool sizes used to manufacture Factor VIII at BPL from 1975 onwards **[BPLL0009120, ep.1]**. Dr Snape appears to have replied to Dr Lane with data on the number of donations in specific batches of Factor VIII manufactured at BPL from 1975-1989 **[ibid, ep.3]**. This data is replicated in **Table 3** below.

28. **Table 3**: Dr Snape's estimates of batch size at BPL from 1975 onwards

| Batch | Year | Approx. weight | No. of donations |
|---|---|---|---|
| - | 1975 | 150kg | 750 |
| HL 1350 | Sept 77 | 450kg | 2,250 |
| HL 2703 | Aug 80 | 600kg | 3,000 |
| HL 2792 | March 81 | 900kg | 4,500 |
| HL 3236 | July 82 | 1,200kg | 6,000 |
| HL 3236 | April 85 | 1,200kg | 6,000 |
| 8Y 3286 | July 85 | 1,200kg | 6,000 |
| 8Y 3429 | Nov 86 | 1,400kg | 7,000 |
| FHC 0001 | Feb 88 | 2,400kg | 10,000 |
| FHC 0027 | June 88 | 3,200kg | 13,500 |
| FHC 0082 | Dec 88 | 3,400kg | 14,500 |
| FHC 0178 | July 89 | 3,400kg | 14,500 |

29. **Table 3** indicates that the pool sizes used to manufacture BPL Factor VIII increased significantly - by around 1,900% - from 750 donations in 1975 to 14,500 donations by 1989.

"*Batch histories*"

30. A set of documents entitled "*batch histories*" are also extant from the HIV Haemophilia Litigation **[CBLA0014475, epp.168-218]**. The "*batch history*" for Factor VIII concentrates contains a comprehensive list of batches of Factor

VIII manufactured at BPL in the years 1978-1988 **[ibid, epp.168-191]**. For each batch, the "*batch history*" provides the year the batch was issued and the approximate number of donations in the plasma pool, along with other information regarding testing and heat treatment.

31. Data derived from the Factor VIII "*batch history*" is shown in **Table 4** below. The "*batch history*" does not show the date on which each batch was issued. For this reason, **Table 4** shows the approximate pool sizes used each year, rather than the pool sizes used on specific dates. Where pool sizes increased during the course of a year, the smaller pool size is dated January and the larger pool size is dated July, to reflect the fact that pool sizes changed on an unknown date during that year.

**Table 4**: "*Batch History*", BPL Factor VIII, 1978-1988

| Year | Approximate no. of donations |
|---|---|
| **1978-1979** | 2,250 |
| **January 1980** | 2,250 |
| **July 1980** | 3,000 |
| **January 1981** | 3,000 |
| **July 1981** | 4,500 |
| **January 1982** | 4,500 |
| **July 1982** | 6,000 |
| **1983-1985** | 6,000 |
| **January 1986** | 6,000 |
| **July 1986** | 7,000 |

| | |
|---|---|
| **1987-1988** | 7,000 |

32. The Factor VIII "*batch history*" **(Table 4)** indicates that the pool sizes used to manufacture BPL Factor VIII concentrates increased by 280%, from 2,250 donations in 1978 to 7,000 donations by 1989. This increase is markedly less than that reported by Dr Snape's estimates **(Table 3)**, in which pool sizes increased by around 1,900% from 1975-1989. Two factors explain the disparity between Dr Snape's estimates **(Table 3)** and the "*batch history*" **(Table 4)**:

    a. The "*batch history*" provides no data for 1975-1978. During this time, Dr Snape's estimates indicate that BPL pool sizes increased by 300%.
    b. The "*batch history*" and Dr Snape's estimates give different figures for 1988: the "*batch history*" states that pool sizes were static at 7,000 donations, while Dr Snape's estimates indicate that pools of 10,000-14,500 donations came into use that year.

33. While Dr Snape's estimates **(Table 3)** and the "*batch history*" **(Table 4)** provide fairly comprehensive data of BPL Factor VIII pool sizes, both data sets are secondary evidence so their reliability may be questioned. Therefore, alternative data is presented below.

Contemporary reports

34. Alternative data on BPL Factor VIII pool sizes can be compiled from contemporary reports made to key committees and personnel. The contemporary reports are not a standardised set of documents. Rather, data has been compiled from an array of material, including correspondence, minutes of meetings, and other documents. What is common to all the material is that a figure as to the pool sizes of BPL Factor VIII was reported to or by key personnel within BPL, the Department of Health and Social Security

(DHSS), the Regional Transfusion Centre Directors (RTDs), or the Haemophilia Centre Directors (HCDs).

35. It should be noted that the documents use a variety of metrics to express pool size. While most documents give the number of donations, other documents give the volume of the pool in litres or kilograms. Where this occurs, the equivalent *(number of donations)* has been calculated as follows:

36. A pool size of 1 litre = approximately 5.55 donations. This is because UK plasma donations were typically 180ml in size: 5.55x180ml = 1 litre. References to a 180ml plasma donation size include:

    a. a report by Dr Maycock, dated 1973 **[CBLA0000154]**;[7]
    b. discussion at the RTD meeting on 20 July 1973 **[CBLA0000153, ep.3, §6];**
    c. the conversions contained in a memorandum from Dr Maycock dated 8 December 1975, in which pool size is expressed in terms of both volume and donations, with a rate of 5.55 donations per litre implied from the figures given **[BPLL0003721]**;
    d. an article published in 1979 by Dr Smith and Dr Bidwell **[CBLA0015427, ep.5]**; and
    e. an article by Dr Gunson, dated November 1986, in which he described trends in blood transfusion in England and Wales **[NHBT0017097, ep.2]**.

37. It should be noted that Dr Snape stated to the Inquiry that UK plasma donations were around 200ml in size **[WITN3431001, ep.76, para.213]**. Dr Lane, in a paper from 1983, implied that the standard donation at that time was 190ml **[CBLA0001779, ep.1]**. For the purposes of this presentation the figure of 180ml is adopted, although it is recognised that there may be some variation in the amount of plasma obtained from donations at different times

[7] For attribution to Dr Maycock, see **CBLA0000024, ep.4**

and in different places. In particular, from 1984 considerably more plasma was removed from whole blood donations where the SAG-M additive was used.[8]

38. A pool size of 1 kilogram = exactly 1 litre. Although 1 litre of plasma in fact weighs 1.05kg, it would appear that BPL fractionators used litres and kilograms interchangeably, such that 1 litre of plasma was equal to 1 kilogram of plasma.[9]

39. A pool size of 1 donor = approximately 1 donation. BPL factor concentrates were produced using plasma pools derived from UK whole blood donations. As explained by Dr T. J. Snape, in the UK *"blood donors [were] asked to give blood less frequently – twice p.a. at that time – so that most fractionation pools would only ever have contained one donation from a given donor"* **[WITN3431001, ep.76-77, para.218]**.

40. It must be stressed that these calculations are only estimates and, therefore, serve merely as an indication of the number of donations in a pool, where the original documents state the size of that pool in litres or kilograms. This is particularly so for conversions from 1984 onwards, when SAG-M was increasingly used.

41. Two further caveats apply to the contemporary reports (this subsection only):

    a. Where the report states that a range of pool sizes were used to manufacture *"NHS factor concentrates"*, it is assumed that the larger pool size refers to BPL, and the smaller size to PFL. For this reason, the larger pool size is included and the smaller pool size is omitted.[10]

---

[8] See Appendix 6 ("The Role of SAG-M in the Plasma Supply in the 1980s") to the Chronological Presentation on Domestic Production and Self-Sufficiency in England and Wales.

[9] See, for instance, the correspondence between Dr J. K. Smith and Dr R.S. Lane in 1982, in which a pool size of 1,200 kilograms **[CBLA0001533]** was taken to equal 1,200 litres **[BPLL0002070].**

[10] This assumption was applied to **CBLA0005371, ep.7, para.8**; **DHSC0001104, ep.2**; and **PRSE0001338**. The assumption was not applied to **CBLA0000840, ep.11**, in which it appears that the smaller pool sizes reported were those used for routine fractionation, whereas the larger pool sizes were used merely for experimental purposes.

b. Where the report gives a minimum pool size which may have been exceeded on occasion, the minimum figure is used as it is the only figure provided.

42. Data derived from contemporary reports is shown in **Table 5** below. Where the documentary material expresses pool sizes in litres, kilograms or donors, the approximate number of donations is *(italicised in brackets)*. It should be noted that it is not always possible to be certain that the figure cited is that of existing pool size at the date of the document, or planned pool size in light of matters discussed in the document.

43. **Table 5**: Contemporary reports, BPL Factor VIII, 1975-1991

| Date | Pool size | Unique ID |
|---|---|---|
| 8 Dec 1975 | 830 donations | **BPLL0003721** |
| 11 Jan 1978 | 2,000+ donations | **CBLA0000711, ep.4** |
| 18 Jan 1978 | 3,000 donations | **CBLA0000715** |
| 1 June 1978 | 400 L *(2,200 donations)* | **CBLA0000801, ep.7** |
| 1 July 1978 | 400 L *(2,200 donations)* | **CBLA0000840, ep.11** |
| 20 Nov 1979 | 600 kg *(3,330 donations)* | **BPLL0002121** |
| August 1980 | 600 kg *(3,330 donations)* | **CBLA0001152, ep.13** |
| 1 Sept 1980 | 5,000 donations[11] | **CBLA0005371, ep.7, para.8** |

[11] The document refers to *"The safety of blood products such as Factor VIII made from large pools (3-5,000 donations) of plasma…"*. It is not clear whether this is intended to describe the then existing situation in BPL, or whether it is a more general comment on the subject matter (screening of donations for hepatitis B). Although this document is a draft, the final report, dated February 1981, contained the same sentence. Dr Lane was a member of the body that drew up the report. **[PRSE0000862, ep.8, §13]**

| | | |
|---|---|---|
| 3 Sept 1980 | 3,500 donations | **HCDO0000553, ep.2-3** |
| 1 Nov 1980 | 3,500 donations | **HCDO0000135_021, ep.4** |
| March 1981 | 2,504 donations | **DHSC0001104, ep.2** |
| 27 April 1981 | 5,000 donations[12] | **CBLA0001342_001, ep.3** |
| 26 Feb 1982 | 3,000+ donations | **HCDO0000270_054, ep.2** |
| 15 April 1985 | 1,200kg (*6,660 dons.)*[13] | **CBLA0002125, ep.1** |
| 26 March 1985 | 7,200 donations | **PRSE0001338** |
| 28 June 1988 | 2,000 L *(11,111 dons.)*[14] | **NHBT0007581, ep.1** |
| 30 April 1990 | 25,000 donations | **BPLL0000934, ep.1** |
| 19 April 1991 | 20,000 donors (*20,000 dons.*) | **NHBT0005266, ep.1** |
| 17 May 1991 | 13,000 donations | **NHBT0005264, ep.1** |

44. **Table 5** indicates that the pool sizes used to manufacture BPL Factor VIII increased by around 3,000%, from 830 donations in 1975 to 25,000 donations in 1990. It is important to note that any inaccuracies in the contemporary reports themselves are replicated in the data.

45. During the course of preparing Dr Lane's draft Proof of Evidence for the HIV litigation, an appendix was compiled setting out evidence of pool sizes

[12] The relevant sentence states that "*virtually all intermediate purity concentrates start with large-scale (500-5,000 donations) cryoprecipitation of FF plasma…*". As the paper discusses international comparators, it is not clear whether the top end of this figure is intended to reflect the then extant position at BPL.

[13] This memo from Mr Prince contains a proposal to increase pool sizes to 1,500kg. The pool size of 1,500kg is not included in the data as it is not clear if the proposal was adopted.

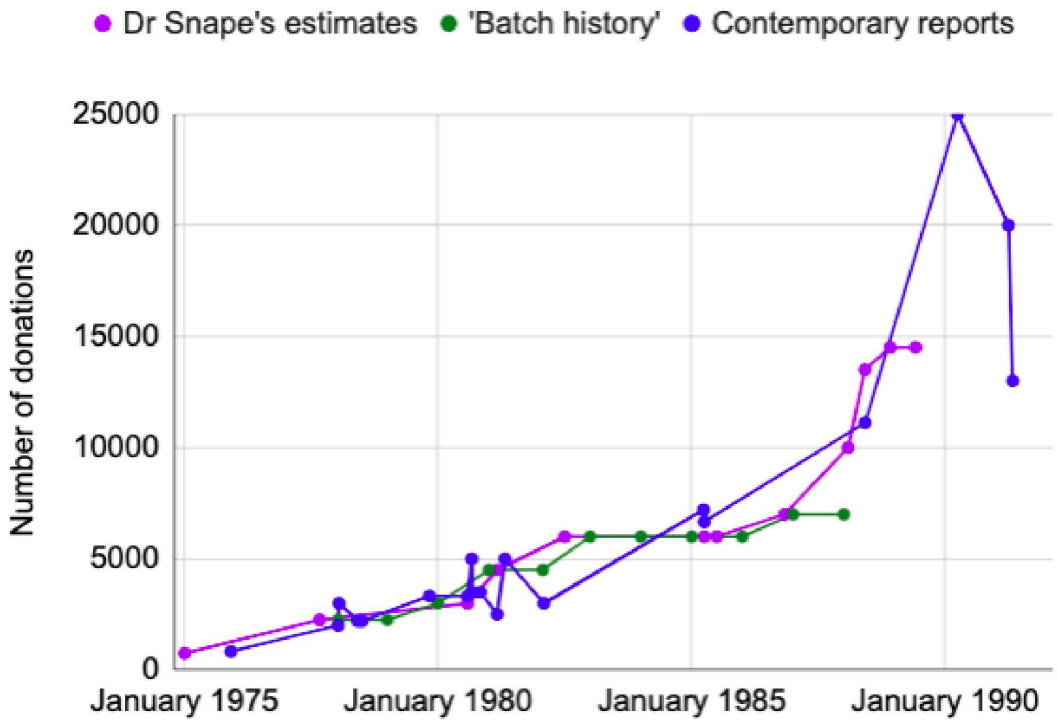
[14] 2,000 litres amounts to 11,111 donations if the conversion rate of 5.55 is used (assuming donations of 180ml). If a different assumption is made, for example, the 275ml of plasma per donation that Dr Gunson said was achievable using SAG-M **[NHBT0017097]**, then the calculated figure of donations is 7,273 donations.

**[CBLA0000004_037; CBLA0000005_002, ep.220, §513]**. This document has been consulted when producing this presentation.

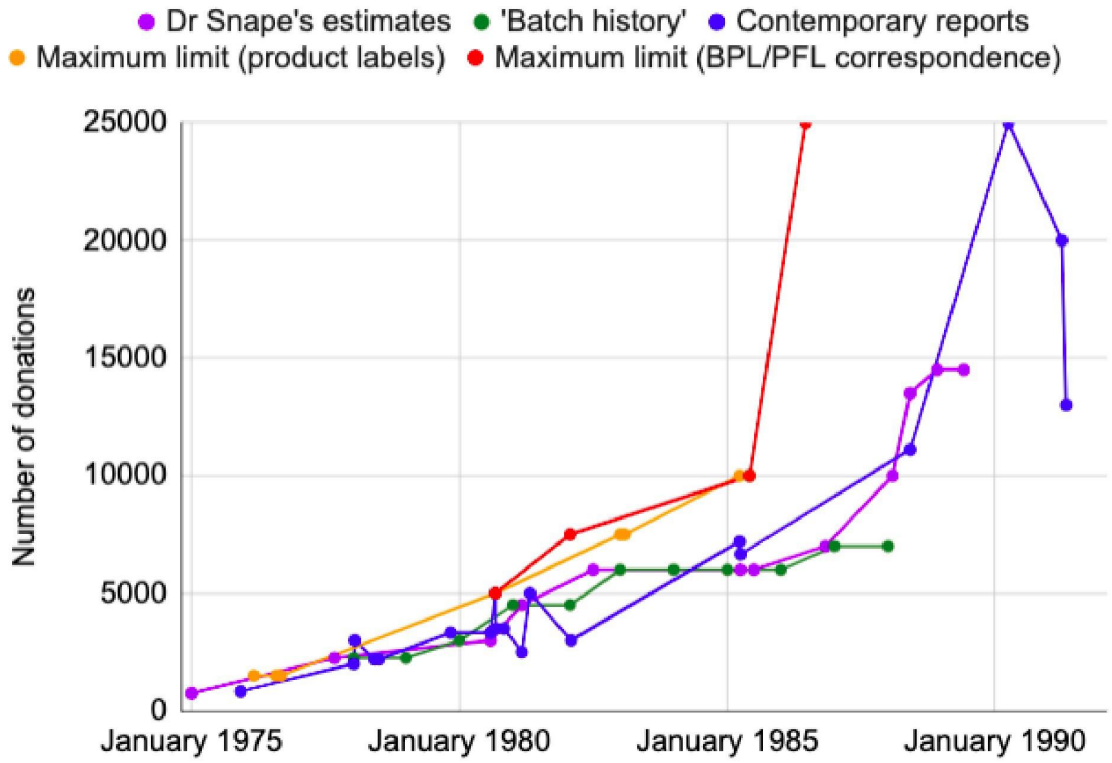
Graphical presentations

46. Data on BPL Factor VIII pool sizes are presented graphically in **Figure 2** overleaf. Combined data showing BPL Factor VIII pool sizes alongside the maximum limits are presented in **Figure 3**.

47. **Figure 2**: BPL Factor VIII: Pool sizes, 1975-1990



48. **Figure 3**: BPL Factor VIII: Pool size and maximum limits, 1975-1990




Pool sizes: BPL Factor IX

49. During the HIV Haemophilia Litigation, Dr Snape did not provide estimates of the pool sizes used to produce BPL Factor IX concentrates.[15]

"*Batch histories*"

50. The "*batch histories*" contain a list of batches of Factor IX concentrate manufactured at BPL **[CBLA0014475, epp.194-196]**. The "*batch history*" for Factor IX is less comprehensive than that for Factor VIII, covering the years

[15] **BPLL0009120**

1983-1987 only.[16] The same data is provided as for Factor VIII: including the year of issue and the approximate number of donations in the pool.

51. Data on the pool sizes of BPL Factor IX derived from the "*batch history*" is shown in **Table 6** below. From 1983-1985, BPL Factor IX, like Factor VIII, was (according to the data) manufactured from consistent pool sizes in each year. However, in 1986-1987, BPL Factor IX was manufactured from various pool sizes in each year. For instance, in 1986, the majority of BPL Factor IX pools contained approximately 6,000 donations, but pools of 14,000, 18,000, 19,000, 21,000, 22,000 and 24,000 donations were also used **[ibid, ep.196]**. For this reason, **Table 6** shows the mode,[17] smallest, and largest pool sizes used to manufacture BPL Factor IX in each year. In this way, **Table 6** captures the variance in BPL Factor IX pool sizes from 1986 onwards.

52. **Table 6**: "*Batch History*", BPL Factor IX, 1983-87

| Year | Mode | Smallest batch | Largest batch |
|---|---|---|---|
| **1983 - 1985** | 6,000 donations | 6,000 donations | 6,000 donations |
| **1986** | 6,000 donations | 6,000 donations | 24,000 donations |
| **1987** | 18,000 donations[18] | 8,000 donations | 20,000 donations |

53. The Factor IX "*batch history*" **(Table 6)** indicates that the average pool sizes used to manufacture BPL Factor IX increased by around 300%, from 6,000 donations in 1983 to 18,000 donations in 1987. It would appear that, in 1986,

[16] The "*batch history*" for BPL Factor VIII covers the years 1978-1988.
[17] The mode is the value which appears most often in a data set. The mode is used because it shows the pool sizes which were most commonly used to manufacture Factor IX concentrate at BPL.
[18] In 1987, the *"batch history"* indicates that pool sizes of both 20,000 donation and 18,000 donations were each used 5 times to manufacture BPL Factor VIII. Therefore, both 18,000 and 20,000 are the modes. The 18,000 figure is used in **Table 6**, rather than the 20,000 figure, because (a) 18,000 is also the median figure (b) 18,000 is closer to the mean figure (17278 donations), and (c) the 20,000 is nevertheless included in the data, as it was the largest pool size used in 1987, as well as the mode.

fractionators at BPL began to experiment with much larger pool sizes of 14,000-24,000 donations and, in 1987, larger pools of around these sizes became the standard.

54. The "*batch history*" for BPL Factor IX concentrates, when compared to that for BPL Factor VIII, indicates that Factor IX pool sizes were larger than those used to manufacture Factor IX. The evidence suggests this may have been due to the practice of pooling multiple Factor VIII pools to produce some batches of Factor IX. For instance, in a memo dated 19 March 1976, Dr Maycock explained that Factor IX pools at PFL were sometimes created from "*2 or 3 subpools*" **[CBLA0000346]**.

Contemporary reports

55. Alternative data on the pool sizes of BPL Factor IX can be compiled from contemporary reports. Data derived from these reports is shown in **Table 7**. The same calculations and assumptions apply to these reports as to those for Factor VIII concentrates. It should also be noted that many contemporary reports state or imply that the pool sizes used to manufacture BPL Factor IX were the same as those used to manufacture Factor VIII. For this reason, many of the documents used within **Table 7** (Factor IX) are the same as those used within **Table 5** (Factor VIII), where it is clear that the report describes the pools used to produce both Factor VIII and Factor IX concentrates.

56. The first document identified by the Inquiry is Dr Bidwell's minute to Dr Maycock of 22 January 1975, which is discussed above. According to Dr Bidwell, it had been agreed that the product labels for BPL Factor VIII and Factor IX would say *"not more than 500 donations"*, rather than referring to specific numbers of donations. However, it had been pointed out to her by Mr Snape that *"batches of Factor IX prepared from the Elstree material correspond to much higher than 500 donations and that the exact number is*

*not known to us."* At PFL small batches were pooled, but the number was again more than 500. Dr Bidwell stated that she told Mr Snape to have *"not more than 1000 donations"* printed, but *"the whole subject of having anything on the label seems difficult. It is certainly not much of a guide to the clinicians any longer."* Dr Bidwell asked to discuss the matter, but the Inquiry has not been able to locate any record of any subsequent discussion **[CBLA0000253]**. Given the absence of further material about the matters raised by Dr Bidwell, no reference is made to this document in **Table 7**.

57. **Table 7**: Contemporary reports, BPL Factor IX, 1978-1988

| Date | Pool size | Unique ID |
|---|---|---|
| 11 Jan 1978 | 2,000+ donations | **CBLA0000711, ep.3** |
| 18 Jan 1978 | 3,000 donations | **CBLA0000715** |
| 1 July 1978 | 400 L *(2,200 donations)* | **CBLA0000840, ep.11** |
| 27 April 1981 | 5,000 donations[19] | **CBLA0001342_001, ep.3** |
| 31 Dec 1984 | 1200 kg *(6,600 donations)* | **CBLA0002173, ep.15**[20] |
| 28 June 1988 | 2,000 L *(11,111 dons.)*[21] | **NHBT0007581, ep.1** |
| 30 April 1990 | 25,000 donations | **BPLL0000934, ep.1** |
| 19 April 1991 | 20k donors (*20,000 dons.*) | **NHBT0005266, ep.1** |

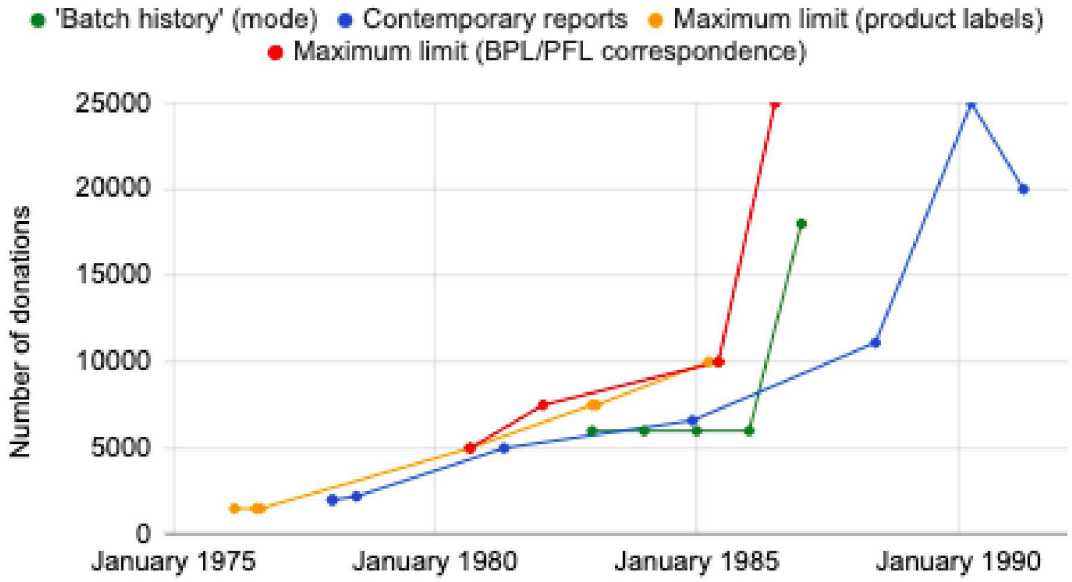
[19] See comments above on this document.
[20] BPL Annual Report: January-December 1984. The report stated that 1,200kg batches of plasma were introduced over the course of the year. Therefore, the pool size is dated 31 December. It is relevant to note that the same report stated that there was a significant increase in the quantity of plasma obtained through the use of SAG-M. As discussed above, this reinforces the need for caution when seeking an approximate calculation of the number of donations contained in a given weight of plasma.
[21] See comments above on the figures cited here.

58. Contemporary reports **(Table 7)** indicate that pool sizes used to manufacture BPL Factor IX concentrates increased by around 1,250%, from over 2,000 donations in 1978 to 25,000 donations in 1990.

Graphical presentations

59. Combined data showing BPL Factor IX pool sizes alongside the maximum limit on the number of donations are presented graphically in **Figure 4** below.

60. **Figure 4**: BPL Factor IX: Pool size and maximum limits, 1975-1990



## Section 3:

## Decisions to increase pool sizes at the Blood Products Laboratory

61. This section examines the reasons underlying decisions to increase pool sizes at BPL throughout the 1970s and 1980s. It is based on what is said on the face of the documents examined by the Inquiry legal team.

The impact of "*self-sufficiency*" and the "*stop-gap*" programme

62. Initial proposals and decisions to increase pool sizes at BPL appear to have been driven, at least in part, by the desire to increase Factor VIII concentrate production in pursuit of "*self-sufficiency*". For instance:

    a. In March 1974, a CBLA note proposed that BPL adopt larger pool sizes of 250 litres[22] in the future, in order to increase production of factor concentrates to 1000 litres per week **[CBLA0000149, ep.1]**.
    b. On 8 December 1975, Dr Maycock stated that BPL Factor VIII pools were derived from 830 donations. Dr Maycock proposed a schedule of increasingly large pool sizes for the following 2 years. He explained that *"as [BPL] increase preparation of Factor VIII concentrate we propose to increase the size of the pool"* **[BPLL0003721]**.

63. Initial decisions to increase pool sizes were justified on the basis that testing for hepatitis B surface antigen (HBsAg) reduced the risk of NHS factor concentrates. For instance:

    a. In his proposal of December 1975, Dr Maycock stated that: "*the large pool size can be defended on the ground that starting plasma and concentrate are tested by RIA*" **[BPLL0003721]**.[23]

[22] (*approx. 1,388 donations)*
[23] It is relevant to note that a report prepared by Dr Waiter comparing NHS Factor VIII with commercial products that was produced a few months later, in March 1976, referred to NHS concentrates as being produced from *"small pools of plasma"* **[CBLA0008747, ep.8]**. This contrasts with Dr Maycock's

b. In a memo dated 19 March 1976, Dr Maycock agreed to the pool size of PFL Factor IX "*being increased to approx. 500L*[24] *...on the understanding that the final pool is prepared from 2 or 3 subpools... each of which has passed its safety tests, including RIA test for the presence of HBsAg*" **[CBLA0000346]**.

64. On 29 March 1976, an application by BPL for a product licence for Factor VIII concentrates stated that *"the maximum pool size foreseen at Elstree is 450 litres (2500 donations)."* The application explained:

> "Because of the large number of control tests which have to be made, there is a trend towards larger pools, in order to lessen the amount of testing and reduce waste of valuable material" **[CBLA0003434, ep.5]**.

65. Subsequently, and as is discussed in the Chronological Presentation and its appendices, BPL was not able to produce sufficient Factor VIII concentrate to meet domestic demand.

66. From late-1977, BPL and the DHSS discussed (and later implemented) the plan for increased production of BPL factor concentrates known as the Stop-Gap programme. On 20th December 1977, Dr Maycock circulated the first Stop-Gap paper to Alec Parrott (DHSS) **[CBLA0000701, ep.1]**. The paper proposed to increase BPL's production of Factor VIII concentrate from 1,200 litres to 2,400 litres over a four-year period **[ibid, ep.4]**. To achieve this, Dr Maycock proposed to increase the pool sizes used to produce factor concentrates at BPL. At the time, pools of 400 litres[25] were used. Dr Maycock proposed to increase these to 600 litres[26] **[ibid, ep.5]**. Dr Maycock also proposed to increase the number of pools fractionated per week from 3 to 4 or 6, *"without increasing working hours"* **[ibid]**.

---

reference to the *"large pool size"* he was proposing. Dr Waiter's paper is discussed in more detail in the Chronological Presentation for England and Wales.

[24] *(approx. 2,775 donations)*

[25] *(approx. 2,220 donations)*

[26] *(approx. 3,330 donations)*

67. In his 5th Draft Proof of Evidence, Dr Lane confirmed that an element of the Stop-Gap programme was an increase in BPL pool sizes to 600 litres **[CBLA0000005_002, ep.66, §165]**. He stated that:

> "The paper dealt with the immediate requirements for increasing Factor VIII production, set against the background of the longer term target for Factor VIII of 1iu per capita as published in the Trends Working Group report.[27] One of the first elements in the Stop-Gap programme was an increase in the pool size from 300 [sic] to 600 litres; a pool size is more efficient in terms of manufacturing practice. Thawing became a continuous process."

68. On 8 September 1978, BPL's annual report for the year ending July 1978, stated that it had been possible to increase pool sizes from 360-400 litres (stated to be ca. 1,800 – 2,000 donations) to 600-650 litres (stated to be 3,000-3,250 donations) **[CBLA0000840, ep.4]**. It had been shown that the larger pool size could be used for *"routine fractionation"* **[ibid, ep.4].**

69. By 7 December 1978, an internal memorandum from Dr Ellis to Dr Lane suggests that production of Factor VIII concentrate at BPL was proceeding "*on the assumption that plasma pools of up to 630 litres are permissible*". This was based on an analysis of the then current label, which permitted a maximum of 3,500 donations (3,500 x 180ml = 630 litres) **[CBLA0000885]**.[28]

Pool sizes at BPL and PFL in the early 1980s

70. On 2 September 1980, Dr J. K. Smith asked Dr Lane for permission to increase the maximum limit on donations per batch at PFL, in order to *"process up to 900kg*[29] *of some plasmas on some days"* **[CBLA0001157].**

---

[27] This report is discussed in the Chronological Presentation for England and Wales.
[28] **CBLA0000885**, a memo from Dr Ellis to Dr Lane, appears to show that the increase in BPL pool sizes to 630 litres was approved at face-to-face meeting, as opposed to a minuted discussion.
[29] *(approx. 4,995 donations)*

71. On 29 September 1980, Dr Lane replied to Dr Smith's memorandum of 2 September. Dr Lane stated **[CBLA0001173]**:

> "I see no reason why the limit on donations per batch should not be lifted, enabling us to process 900-1,000kg[30] of some plasmas on some days. In connection with the risk of hepatitis, I am sure that once one has exceeded the 100-200kg[31] pool-size, one has already exceeded any possibility of small-pool protection. I have discussed this with John Craske and he agrees exactly on this point."[32]

72. Dr Lane made the following remarks about this exchange in his 5th Draft Proof of Evidence **[CBLA0000005_002, ep.219, §511-512]**.

> "[511] The conclusion was based on the belief that the Non-A Non-B virus carrier rate in donors approximated to 1%, and that 100kg of plasma would comprise inputs from a minimum of 200 donors.
>
> [522] From a fractionator's point of view, it is, in any event, necessary to pool plasma to manufacture concentrate and there are several reasons why large pools are preferable to small ones from a manufacturing standpoint. The most obvious is the economy of scale which this brings to the production process. Second, very small pools do not provide enough product for severe haemophiliacs who would very quickly exhaust Factor VIII or Factor IX concentrate produced in such a way, requiring product from another pool thereby defeating the object of a small pool approach. Thirdly, the administrative aspects of establishing and running small pools on any scale would be quite disproportionate to the amount of product such methods could produce. Fourthly, large pools have the effect of producing a more standardised (and more predictable) product in terms of quality. By way of explanation of this point, we found enormous variations in the Factor VIII content of plasma provided to us by different Regional Transfusion Centres and the pooling process itself eliminated these peaks and troughs which would otherwise have complicated the manufacturing process."

---

[30] *(approx. 4,995 - 5,550 donations)*
[31] *(approx. 555 - 1,110 donations)*
[32] The Inquiry has found no contemporary record of a discussion between Dr Lane and Dr Craske on this point.

73. The planning for the full redevelopment of BPL appears to have proceeded on the basis of at least providing for the possibility of increasing pool sizes to pursue national self-sufficiency. On 1 September 1980, a paper by L. Vallet set out plans for a new BPL plant capable of processing 450,000 litres of plasma per annum **[CBLA0012351, epp.14-17]**. The paper stated:

> "There will be an advantage in constructing the plant in the form of two… fractionation units operating side by side, each taking 5,000 litres weekly… This provides at maximum capacity for four pools of 2,500 litres[33] to be taken weekly" **[ibid, ep.15]**.

74. In 1980, the Protein Fractionation Technology Working Party ("PFT") made initial recommendations to increase plasma processing to 450,000 litres per year **[CBLA0012351, ep.1]**. The PFT concluded that fractionation would continue to be based on cold ethanol precipitation and included Mr Vallet's proposals as one option to achieve the increased production target **[ibid]**. The PFT submitted final recommendations to the DHSS in early 1981 **[DHSC0002213_021]**. The recommendations appear to be based on Mr Vallet's proposal for twin fractionation units, each equipped with centrifuges up to 2,500 litres in capacity. The recommendations stated:

    a. *"fractionation should continue to be centred on cold ethanol precipitation"* **[DHSC0002213_021, ep.1]**.
    b. the PFT considered that *"a twin precipitation facility would be appropriate"* **[DHSC0002213_021, ep.11]**.

75. As the Inquiry has heard, plans for the redevelopment of BPL remained undecided for some time. It appears that the PFT's proposals to continue using cold ethanol precipitation at the redeveloped BPL were accepted by the Policy Steering Group ("PSG") on the redevelopment of BPL in July 1982 **[CBLA0001606, ep.3]**. Therefore, it seems likely that Mr Vallet's proposals to manufacture BPL factor concentrates using pools of 2,500 litres were

[33] *(approx. 27,750 donations)*

ultimately accepted by the PSG, and subsequently the DHSS, albeit after a delay.

76. On 13 January 1982, Dr Smith wrote to Dr Lane requesting permission to increase the permissible effective pool size for Factor VIII and Factor IX to the equivalent of 1,200kg or 7,500 donations with immediate effect **[CBLA0001533]**. He stated that this change:

> "would allow us to:
> (1) make the most effective use of freeze drying plant.
> (2) test timings for the ultimate pool size for a new BPL.
> (3) recover more rapidly from processing losses to be incurred during the CF and Technical Services upgradings.
> (4) test new processing equipment at design capacity."

77. Dr Smith added that: *"This will probably be the last request for an increase in pool size until the yield of factor VIII is increased really significantly."* As has been noted, Dr Smith referred to the need to adjust both BPL and PFL labels and quality control documentation accordingly. Dr Lane approved the change on 25 January 1989 **[BPLL0002070]**.[34]

78. As seen in **Section 1**, from 1983 to 1985 pool sizes at BPL appear to have been held constant, at a size of up to 7,500 donations.[35] As is discussed in the Chronological Presentation on England and Wales, during this time BPL and PFL developed heat-treated Factor VIII, and later Factor IX concentrates.

79. In early-1985, as BPL scaled up heat-treated Factor VIII concentrates from experimental to full-scale production, smaller pool sizes were briefly used. In January 1985, an early batch of heat treated 8Y was produced from a pool of

[34] The terms of Dr Lane's authorisation refer only to Factor VIII. It is not known whether this was intentional.
[35] As seen above, pool sizes of up to 7,500 litres were requested by Dr Snape and approved by Dr Lane in January 1982 **[CBLA0001533** and **BPLL0002070]**.

600kg[36] **[CBLA0001993, ep.1]**. By 15 April 1985, a memo by Mr Prince indicates that batches of 8Y were produced from 1,200kg[37] pools **[CBLA0002125, ep.1]**. Mr Prince proposed to increase this pool size to 1,500kg[38] *"in order to bring through put of plasma back to the HL levels"* **[ibid]**.

80. Later in 1985, BPL began to plan further increases in pool sizes. On 10 June 1985, in a reply to a memo from Mr Prince,[39] Dr Snape stated:

> "I have assumed that a limit of 10,000 donations maximum will not restrict operations in the present building, but that an extension to 20,000 donations maximum will be required for the new facility. The higher figure will be used in any product licence application." **[CBLA0002190]**.

81. On 20 June 1986, Dr Snape wrote again to Mr Prince. He stated:

> "Dr Lane has agreed that the maximum pool size may be extended to 25,000 donations for heat-treated coagulation factor concentrates. The appropriate label revisions will be made as soon as possible. Please check that any manufacturing documentation is revised before the increased limit is implemented." **[CBLA0004791]**.

82. On the same day, Dr Snape wrote to Dr A. Smithies (DHSS).[40] He stated:

> "I am writing to advise you of a proposed change in donor pool size limitation for BPL (and PFL) coagulation factor concentrates. It is proposed to increase the maximum number of donations to be pooled from 10,000 to 25,000 plasma donations. In taking this decision we were mindful of the terminal heat treatment of coagulation factor concentrates made from such pools and the fact that any increase beyond the already large 10,000 donor limit is probably not significant. I thought you should be aware of this proposal" **[DHSC0002303_027]**.

---

[36] *(approx. 3,330 donations)*. This figure is not included in the data in Section 2 as it is not clear that a pool of this size was used to manufacture 8Y on any other occasion.
[37] (approx. 6,660 donations)
[38] (approx. 8,325 donations)
[39] The Inquiry legal team has been unable to find any copy of Mr Prince's memo dated 25 April 1985.
[40] The Inquiry legal team has been unable to find a response from the DHSS to Dr Snape's letter.

83. The practice of printing the maximum number of donations on BPL product labels ceased once donations passed 10,000 (see **Table 1)**. Although one document suggests that this change took place in or around February 1987 **[BPLL0002039]**, the Inquiry legal team have been unable to confirm that date or find documentation explaining the reasons for the change.

## Section 4:
## Conclusions

84. **Section 2** of this presentation indicates that the pool sizes used to produce factor concentrates at BPL increased substantially throughout the 1970s and 1980s.

85. During this time, pool sizes at BPL were circumscribed by a "*maximum limit*" on the number of donations in each pool. Two types of evidence have been used to assess the maximum limit: product labels and correspondence between BPL and PFL. Both forms of evidence indicate that the maximum limit was increased substantially throughout the 1970s and 1980s.

86. **Section 2** indicates that the size of the pools used to produce BPL Factor VIII concentrates increased significantly. Three types of evidence are examined: Dr Snape's estimates, the Factor VIII "*batch history*", and contemporary reports made to key committees or personnel.

87. The evidence indicates that BPL Factor VIII concentrate was produced from increasingly large pools during the 1970s and 1980s. The "*batch history*" indicates that Factor VIII pool sizes increased by 280%, from 2,250 donations in 1978 to 7,000 donations by 1989. Contemporary reports indicate that BPL pool sizes increased by 3,000%, from 830 donations in 1975 to up to 25,000 donations in 1990.

88. The size of the pools used to produce Factor IX concentrates at BPL also increased substantially. Two types of evidence are available: the Factor IX "*batch history*" and contemporary reports. The Factor IX "*batch history*" indicates that Factor IX pool sizes increased by around 300%, from 6,000 donations in 1983 to 18,000 donations in 1987. Contemporary reports indicate that Factor IX pool sizes increased by around 1,250%, from around 2,000 donations in 1978 to up to 25,000 donations in 1990.

89. **Section 3** of this presentation considered the documentary evidence of the reasons given for increasing the pool sizes. The documents suggest that a number of factors were involved, which are set out below. It is important to note that these interpretations are based solely on what appears on the face of the documents, and that additional, or alternative, analyses are available.

90. From 1975, onwards decisions to increase pool sizes were taken in order to increase domestic production of factor concentrates with the resources then available. The efficiencies of larger pools were stressed in some of the post-facto explanations.

91. Initially, larger pool sizes were defended on the grounds that hepatitis B testing was effective in reducing the risk of hepatitis. As evidence of NANB emerged, a further rationale for increased pool sizes was put forward: the proposition that, over a pool size of around 100-200kg, there was no significant increase in risk as the benefits of "*small pool protection*" against NANB infection had already been lost.

92. Later, the availability of other methods to reduce risk fostered the use of larger pools. As heat-treated factor concentrates were developed and shown to be effective, at least against AIDS, BPL pool sizes began to increase after a period in which they had been maintained at a level. Later increases may have been related to the redevelopment of BPL.

**Tom Dunning, Inquiry Legal Team**
**Matthew Hill, Counsel to the Inquiry**
**March 2022**