Chronological Presentation on the Domestic Supply of Blood Products in England and Wales

Appendix 5

The Role of the Single Donor Plasma Pack in Plasma Supply in the 1970s and 1980s

Introduction

1. This Appendix reviews the introduction of the use of single plasma packs (SPPs) in providing fresh frozen plasma (FFP) to the Blood Products Laboratory (BPL) in the late 1970s and early 1980s.

2. SPPs were intended to supplement and eventually replace 5-litre packs that were, by the late 1970s, the main method by which plasma was shipped to BPL. The 5-litre packs had themselves superseded collection in glass bottles (see **Appendix 3** for further discussion of this process in some regions). 5-litre pooling required the individual packs of plasma separated from whole blood to be opened at the Regional Transfusion Centres (RTCs) and pooled into 5-litre bags. This was an 'open' system as the plasma was exposed at RTCs during the pooling process. SPPs were designed to enable single donations of plasma to be sent to BPL for fractionation, thereby maintaining a 'closed' system so that the plasma would not be exposed until pooled at BPL. Such a system accorded to the principles of good manufacturing practice laid down by the Medicines Inspectorate.[1]

[1] Paper, date and author unknown, **NHBT0100836_017**

3. Although the risk of bacteriological contamination was one reason for the move to a closed system, the focus in this Appendix will be on the SPPs' role in plasma supply. The SPP was designed specifically to receive FFP for fractionation, and it was hoped that this would improve both the efficiency and quality of plasma collection by RTCs, and hence play a role in increasing supplies to BPL as part of the Stop-Gap/MARP01 plan.

4. SPPs do appear to have played a role in increasing the plasma supplies in the early 1980s, although it is difficult to quantify that role or assess its significance. Within a few years, the advent of the SAG-M additive to Red Cell Concentrates had increased the amount of plasma that could be extracted from a donation, rendering the original SPPs too small. As is discussed in **Appendix 6**, a new bag was developed. This eclipsed SPPs both in terms of usage and influence in increasing plasma supplies.

The origins of SPP

5. As is discussed in the main presentation, ministers decided in the 1970s that state bodies, including BPL and Regional Transfusion Centres, should be subject to the same principles as commercial entities in respect of the Medicines Act 1968. This included inspection by the Medicines Inspectorate, albeit with some qualifications as to how any shortcomings would be addressed. Following initial inspections it had become apparent by mid-1977 that the existing system of plasma collection into 5-litre packs was not compatible with good manufacturing practice unless the 'open' pooling of the plasma donations took place in aseptic units. Such units would be expensive to develop. The use of SPPs, or an equivalent 'closed' system for separating and handling plasma, was seen as a preferable alternative.[2]

6. Dr Lane, then Director Designate of BPL, considered that there were further advantages to the use of SPPs, and indeed saw these as integral to the Stop-

[2] Minutes of the 166th Regional Transfusion Directors', 4 May 1977, **DHSC0002367_012**, pg. 5; John Flint to Dr Fletcher, 27 May 1977, **BPLL0004236**, pg. 7. All reference to page numbers in this Appendix are to electronic page numbers unless otherwise stated. These may or may not correspond to the internal parge numbers of the documents.

Gap proposals for the interim redevelopment of BPL.[3] In a paper dated September 1977, Dr Lane argued that the adoption of SPPs would bring the following benefits for both RTCs and BPL.[4]

- 'Open system' processing at RTCs would become minimal and there would be a corresponding reduction in the need for redevelopment and capital expenditure for clean and sterile areas.
- Staff workload would be reduced.
- The time limits imposed by pooling fresh plasma for factor VIII as part of the general schedule for blood component production would be removed for the daily regional service (i.e. plasma could be treated according to its own requirements, and not by those that applied to platelets, cell concentrates, cryoprecipitate or other blood components).
- SPPs could be tested at the RTCs for hepatitis B surface antigen (HBsAg) using the most sensitive test then available, RIA. This would be more sensitive than the existing process of testing the 5-litre packs at BPL, would prevent the waste caused by having to discard a pool of plasma because of one infected donor, and would allow for identification of infected donors.
- Single pack units would not have to be screened for bacteriological infection on arrival at BPL as they would have been produced in a closed system.
- Single pack units were suited to rapid thawing which improved the yield of factor VIII. Dr Lane noted the standard yield of 300-350 iu/ litre compared with yields of 500+ iu/ litre from the quick thaw process - an increase of almost 60%.

7. Dr Lane's paper acknowledged that moves to SPPs would necessitate changes at BPL, which would be costly. These included alterations to storage facilities and production methods. However, BPL had to be redeveloped in any event and, in Dr Lane's view, it made more sense to incur such capital costs at one site rather than in all 14 RTCs.[5]

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[3] The Stop-Gap programme, and its successor MARP01, are discussed in the main presentation.
[4] Dr Lane 'Redevelopment of the Blood Products Laboratory within an Integrated National Blood Transfusion Service', September 1977, **CBLA0000664_007**, pg.3-4
[5] **CBLA0000664_007**, pg. 4

8. Dr Lane's paper was discussed at the NBTS Central Committee's Sub-Committee on the Central Laboratories on 18 November 1977. Dr Jenkins said it would be supported by most Regional Transfusion Directors (RTDs) on the grounds that it would obviate the need for substantial upgrading of RTC processing areas and delays in processing, with the consequent loss of active factor, would be minimised.[6] Dr Maycock expected the change-over could take three to five years, which would assist RTDs in planning modifications to their centres.[7] The Sub-Committee agreed that the proposed change was desirable and that their view should be reported to the Central Committee. Dr Lane later wrote in his 5th Draft Proof of Evidence that the report he had written generated limited response from the Department of Health but that steps were taken to phase out the 5-litre packs in favour of single donor ones.[8]

9. A further meeting held in October between the DHSS officials, Dr Lane and Dr Maycock, and four directors of RTCs agreed that pooling would be phased out and BPL would modify their procedures to accept supplies of plasma as single units.[9]

SPPs and the redevelopment of BPL

10. The switch to SPPs from 5-litre packs was included as part of the planning assumptions that underlay the Stop-Gap programme of interim redevelopment at BPL. This programme is discussed in the main presentation and in **Appendix 1 and 2**. For the purposes of this document, it is sufficient to note that the change from stage 1 of Stop-Gap to stage 2 was intended to coincide with the greater use of SPPs, and that it was anticipated that this would assist in increasing plasma supply and processing capacity at BPL from 1,800 litres to 2,400 litres per week. The original Stop-Gap paper, prepared in December

[6] Minutes of the Central Committee for the NBTS Sub-Committee on the Central Laboratories, 18 November 1977, **DHSC0002185_038**, para 4.2
[7] **DHSC0002185_038**, para 4.2
[8] Dr Lane's 5th Draft Proof of Evidence, 1990, **CBLA0000005_002**, para 156
[9] John Flint, Note of a meeting to discuss standards of processing of blood and blood products and the manufacture of sterile fluids in the Regional Blood Transfusion Service, held 6 October 1977, **CBLA0004181**

1977, proposed a four-year time period to achieve to complete this work (i.e. by 1982). The paper referred to the experience of N.E. Thames RTC, which had reported an increase in the capture of FPP from 35,000 units per annum to 60-70,000 units once 5-litre pooling was discontinued.[10]

11. Dr Lane's suggestion that SPPs would prove efficient in terms of saving time and resource in RTCs appeared to be borne out in several centres in 1978. Leeds, Southampton and Liverpool all reported that they would be able to send more FFP to BPL were it to accept single packs rather than 5-litre pools.[11]

12. For BPL, the increased use of SPPs necessitated the installation of an automated system to allow bags to be opened mechanically.[12] In a paper written in June 1978, Dr Lane estimated that to create a standard factor VIII pool of 400 litres, 2,000 single bags would need to be opened at a rate approaching 2 per second.[13] The changeover to transfer in SPPs would need to be phased in over two or three years and Dr Lane proposed forming a working group to address difficulties arising in both BPL and RTCs.[14] Following an RTD meeting in July, the Single Packs Committee was formed, composed of one representative from each regional grouping of RTDs and Dr Lane. Representatives of the DHSS, Dr Waiter and Mr Dutton, would receive papers and have the option of attending.[15] Documents from this time show Mr Dutton and the DHSS taking an interest in this matter and its resource implications. [16] [17]

13. In November 1978 Dr Lane and Dr Cleghorn visited Travenol at their headquarters in Illinois to discuss the development of a new bag to be used

[10] Stop-Gap requirements for Factor VIII production 1978 to 1982, December 1977, **CBLA0000701**, in particular pg. 4 and pg.8
[11] Table, Supply of Fresh Frozen Plasma by RTCs, April – September 1978 **CBLA0000743**
[12] **SBTS0000288_036**, pg. 2
[13] **SBTS0000288_036**, pg. 2
[14] **SBTS0000288_036**, pg. 3
[15] Note of a Meeting of English RTDs, 5 July 1978, **SCGV0000072_016**, pg. 2
[16] Minute from T. Dutton to Mr. Parrott, 4 July 1978, **DHSC0002325_032**
[17] Note of a Meeting of English RTDs, 5 July 1978, **SCGV0000072_016**, pg. 2

as a SPP. [18] A prototype was reviewed by the Single Bag Committee in June 1979, which also considered a proposal for an automated opening system that would allow for a 1,000 litre pool of plasma to be opened by a single machine in approximately 1.5 hours.[19] Travenol subsequently produced the International Plasma Pack for single donor plasma, which was widely used in England and Wales.

14. To accommodate single unit FFP there was also a need for increased deep freeze storage at BPL, something that formed part of the ongoing plans for the Stop-Gap programme.[20] A modular cold store designed for SPPs was completed and commissioned by December 1980.[21]

The Introduction of SPP

15. Regional trials of 6,000 SPPs developed in association with Travenol appear to have begun in late 1980,[22] and were expanded in 1981.[23] In a paper written ahead of those trials, Dr Lane anticipated that other manufacturers of plastic bags may also want to "follow the lead taken by Travenol", something that he described as being acceptable as long as they met the relevant technical and manufacturing requirements.[24] Despite this, concerns were later raised that Travenol was seeking to establish a monopoly, something that Dr Lane and the Single Pack Committee denied.[25] [26]

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[18] Report: 'Increased provision of fresh frozen plasma for Factor VIII: improvement in design of the Fenwal Blood Pack System', 1978, **CBLA0001044**, pg. 5
[19] Dr Lane, 'Single Bag Committee: Progress Review for the RTD Meeting', 27 June 1979, **DHSC0003728_084**, pg. 1
[20] Dr Lane 'The Function of Stop-Gap and Phased Redevelopment of the Blood Products Laboratory', 31 May 1979, **BPLL0001508**, pg. 33, pg.36
[21] Dr Lane, 'Blood Products Laboratory: A summary of performance since September 1979', 4 February 1981, **CBLA0001258**, pg. 7
[22] Dr Lane 'Plasma Fractionation Working Party', 16 September 1980, **CBLA0001153**, pg. 3
[23] Plasma supply for self-sufficiency in Blood Products, a discussion document by R. S. Lane and H. H. Gunson for the Ad Hoc Working Party on Trends in Blood Transfusion, [date unknown] **CBLA0002451**, pg. 7
[24] Dr Lane 'Plasma Fractionation Working Party', 16 September 1980, **CBLA0001153**, pg. 3
[25] Meeting Minutes of the Eastern Division, Consultant Haematologists in the BTS, held 6 May 1981, **NHBT0092845_041**, pg. 2
[26] Minutes of the Single Packs Committee Meeting, held 4 September 1981, **SBTS0000291_054**, pg.1

16. In his paper in 1980, Dr Lane reiterated what he saw as the advantages of SPPs:[27]

> "In summary, the SPP allows:
>
> (i) collection of blood and FFP in a 'closed system' of packs at RTCs and sets aside the need to meet Medicines Division requirements for handling 'open system' for FFP collection in 5L pools.
>
> (ii) It eliminates time-consuming pooling of FFP into 5L packs at regional centres.
>
> (iii) The SPP is not a multi-purpose unit, thus its use establishes an immediate commitment of the plasma to fractionations, encouraging a contractual approach to the support of central fractionation and standardization FFP quality.
>
> (iv) The SPP allows for more rapid freezing of plasma.
>
> (v) There is positive identification of each donor immediately before fractionation. This control requirement may become essential for regulatory purposes.
>
> (vi) The SPP will incorporate the bar-code system of pack and donor identification in control procedures at BPL and into pre- and post-quarantine cold storage.
>
> (vii) The SPP is designed for automated opening at BPL allowing rapid accumulation of FFP in collecting systems with a high degree of environmental protection of both feedstock and operator…"

17. At a meeting of RTDs in March 1981, Dr Lane reported that revised SPPs would be available for use by RTCs towards the end of the year.[28] It appears, though, that there was some slippage of anticipated timetables in the months that followed. The automated bag opening machine had been expected to be commissioned by August that year, with production scaled up to "complete operations with single packs" in March/April 1982.[29] By September, the Single Packs Committee was informed by its Chairman, Dr Wagstaff, that the timetable had slipped and that the main single plasma pack programme was not anticipated to commence until the end of October or early November. This was associated with delays to the completion of phase 1 of the redevelopment

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[27] Dr Lane 'Plasma Fractionation Working Party', 16 September 1980, **CBLA0001153**, pg. 3-4

[28] Minutes of 181st RTD Meeting, held 17 March 1981, **NHBT0018341**, pg. 4; this timescale is supported by Response to Medicines Division Report, 5-6 March 1981, **DHSC0002209_004**, pg. 7

[29] P.R. Foster, Report on the Symposium 'Advances in Blood Transfusion Practice', May 1981, **SBTS0000480_048**, pg. 3

of BPL.[30] At a meeting of RTDs in February 1982, Dr Lane stated that the automated "tear-down" opening equipment would "soon be in operation".[31] It appears that the machine was up and running by mid-1982.[32]

18. The problems in transition were felt in RTCs as well as at BPL. In a minute dated 24 May 1982, Mr Howell wrote to Dr Gunson about the latter's request to increase the production of FFP at Manchester RTC. Mr Howell wrote that "the availability of International Plasma Packs from Travenol is still suspect and there are still continuing problems of storage and handling at [BPL]." As a consequence, Mr Howell had agreed with Dr Smith of BPL that BPL would accept "50% of our proposed target of special packs [seemingly a reference to SPP] and an increased amount of FFP in 5-litre packs." He commented that BPL had at that time "considerable problems with a large accumulation of special single plasma packs." Dr Smith hoped to be able to receive the bulk of Manchester's SPPs by July.[33]

19. Despite these problems, it is clear that SPPs began to be provided to BPL in this period. In BPL's Annual Report for 1981/82, Dr Lane wrote that FFP input had increased for the first time in five years,[34] and was 26% greater than in 1980/81.[35] In the period from October 1981 to April 1982, and in particular in the final three months of that time, "a significant quantity of [FFP] was in single donor packs." He anticipated "significant progress" to be made in the automation of plasma processing in the year to come.

20. Dr Lane did not seek to quantify the effect of the increased use of SPPs on the increase in plasma supply. It is important to recall that the pro-rata scheme for the distribution of blood products was introduced in the same year, something that is discussed in the main presentation and **Appendix 4**.

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[30] Minutes of the Single Packs Committee Meeting, held 4 September 1981, **SBTS0000291_054**, pg.2
[31] Minutes of the 184th RTD Meeting, held 18 February 1982, **CBLA0001551**, pg. 5
[32] BPL Annual Report, April 1982-December 1983, 16 January 1984, **DHSC0002239_003**, pg. 6, where reference is made to the machine "operating successfully for 18 months"
[33] Memo from Mr Howell to Dr Gunson Re: Increased Production of FFP, 24 May 1982, **NHBT0094638**, pg. 1
[34] BPL Annual Report 1981/82, 20 April 1982, **CBLA0001570**, pg. 2
[35] **CBLA0001570**, pg. 4

21. At the September 1982 RTD meeting, Dr Lane reported that capacity would be increased in October to allow the second phase of the SPP programme to continue, which would allow reception of more than the total current annual plasma supplied.[36] After one further meeting the single pack working party could be disbanded to be reconvened only on an ad hoc basis.[37]

22. There is some evidence to suggest that during 1982 and 1983 SPPs played a role in increasing the plasma supply to BPL, although it is again difficult to determine how significant that role was when compared to other factors (including pro-rata distribution). The First Annual Report to the CBLA, which covered December 1982 to December 1983, recorded that the input of FFP had risen to 150,000 kg per year, equal to BPL's maximum fractionating capacity at that time.[38] It noted the continued successful operation of the automated pack-opening machine and the considerable efforts made to establish the SPP as the standard method for transport and storage of FFP.[39] Similar observations were made in the BPL Annual Report for the period from April 1982 to December 1983, which also recorded that in the previous 12 months (i.e. from December 1982) 650,000 single plasma units had been receive.[40]

23. At a regional level, the Northern RHA reported that the increase in the amount of FFP sent to BPL had been reflected in a greater pro-rata return of factor VIII and albumin from Elstree (6,435 units in 1983 compared to 4,360 units in 1981). The report credited the use of the SPP with improving the quality of plasma, resulting in increased yields.[41]

The effect of SAG-M

[36] Minutes of the 186th RTD Meeting, held 20 September 1982, **CBLA0001623**, pg. 7
[37] **CBLA0001623**, pg. 7
[38] First Annual Report to the Central Blood Laboratories Authority: December 1982 - December 1983, **BPLL0002401**, pg. 13
[39] First Annual Report to the Central Blood Laboratories Authority: December 1982 - December 1983, **BPLL0002401**, pg. 13
[40] BPL Annual Report: April 1982-December 1983, 16 January 1984, **DHSC0002239_003**, pg. 6
[41] Northern Regional health authority Annual Programme 1984/85 and 1985/86, **TYWE0000042**, pg. 2

24. As is discussed in **Appendix 6**, by 1983 thought was being given to the use of SAG-M additives to Red Cell Concentrates, which would allow for large amounts of plasma to be obtained from an individual donation. This posed difficulties for the original International Plasma Pack produced by Travenol, which would no longer be large enough.[42] As SAG-M became increasingly used, a distinction grew in terminology between plasma classified as SPP (i.e. that obtained using the original International Plasma Pack, or packs of similar size), and that classified as having been obtained through the use of SAG-M. While this was no doubt helpful for planning purposes, the two systems should not be seen in absolute contradistinction. The principle of using a single pack for a single donor's plasma was retained.

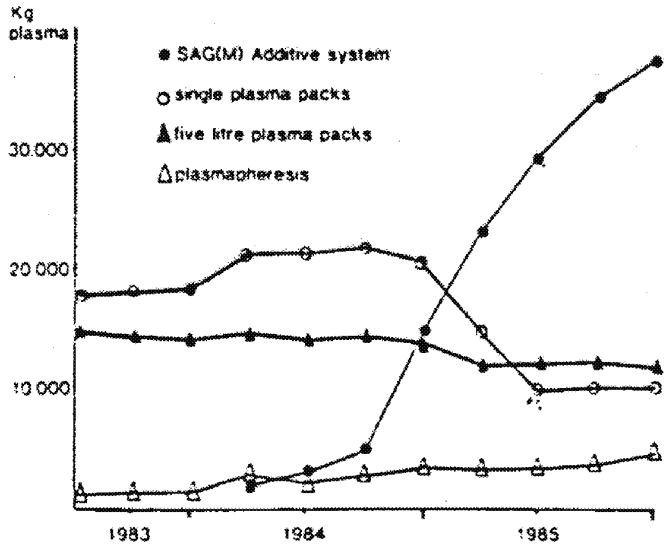
25. That said, the increased role for SAG-M prefaced a decline in significance for SPP plasma. While around half the FFP input to BPL came from SPPs in 1984, there was no significant increase in plasma supply until the introduction of SAG-M. BPL's Annual Report for the (calendar) year noted that plasma supply remained at 1983 levels for most of 1984, only rising in the last quarter and into 1985 due to increasing collection of donations using SAG-M.[43] Figures for the year show the percentage of SPP FFP declined from 57.5% of the total plasma input in the first quarter to 43.4% in the final quarter.[44] 5-litre plasma pack receipts also fell significantly in the same period (from 41.2% to 26.2%). SAG-M receipts rose dramatically, from 8.5% in the third quarter of 1984 to just over 30% in the final quarter.[45] As well as showing the growth of SAG-M, these figure demonstrate that SPPs had not completely displaced 5-litre packs even by the end of 1984.

26. An article by Dr Gunson published in November 1986 concluded that the increase of plasma obtained from SAG-M donations had come largely at the

[42] H.H. Gunson, 'Trends in blood transfusion practice in England and Wales', published November 1986 in Health Trends, **NHBT0017097**, pg. 2-3
[43] BPL Annual Report: January-December 1984, April 1985, **BPLL0004123**, pg. 8
[44] **BPLL0004123**, pg. 13
[45] **BPLL0004123**, pg. 13

expense of separation of plasma into SPPs.[46] He supported his argument by reference to the following graph.

The changing pattern of the methods for fresh plasma collection in England and Wales, three-monthly statistics, 1983-1985.[47]

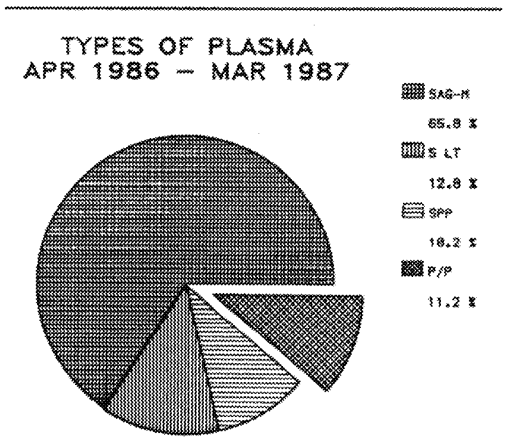


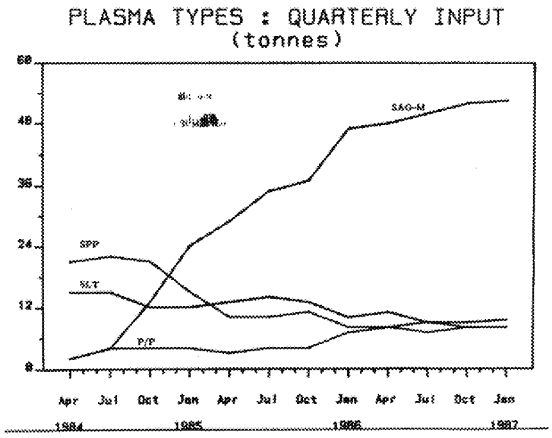
27. The graph shows both that SPP input declined from 1984 with the rise of SAG-M and that by 1985 it had even fallen below the input from 5-litre packs.

28. Dr Gunson's thesis, and the data in the graph, are supported by the minutes of an October RTD meeting which noted that while SPP plasma had accounted for 50% of input to BPL in July to September 1984, it fell to only 16% in the same quarter in 1985. During the same period, 5-litre packs had shown an initial fall in real term input but then rose to 24% of the total input. SAG-M plasma input had also risen, from only 8% in the period July to September 1984 to 55% of the total plasma input in the same period in 1985.[48]

[46] **NHBT0017097**, pg. 5
[47] Graph from H.H. Gunson, 'Trends in blood transfusion practice in England and Wales', published November 1986 in Health Trends, **NHBT0017097**, pg. 4
[48] Notes of the RTDs' Meeting, held 8 October 1985, **CBLA0002263**, pg. 11

29. This trend continued into 1986 and 1987. The BPL Annual Report for April 1986 to March 1987 showed the distribution of FFP received from plasmapheresis, SPP, 5-litre pooled plasma and the SAG-M pack in the following diagrams. [49]





30. These data support other evidence suggesting SPP input started to fall in October 1984 and 5-litre pooled plasma input slowly increased at this time. By around March 1985, 5-litre packs look to have been providing more plasma to BPL than the SPPs which continued to decline, albeit less dramatically. By 1986/87, more plasma was provided to BPL by each of the other methods and SPPs provided just 10% of the total.

Conclusion

[49] BPL Annual Report, April 1986-March 1987, **CBLA0002371**, pg. 6, pg. 9, p.10

31. The change from 5-litre plasma pooling to the use of a single donation plasma pack, designed specifically for FFP to be fractionated, formed part of the drive to double plasma intake in the Stop-Gap programme by increasing the quantity and quality of plasma separated from whole blood donations at RTCs. Dr Lane put forward a number of advantages centred around improving quality of the plasma input to BPL and avoiding the need to upgrade RTC facilities to comply with the Medicines Act.

32. Updates to BPL were required to enable receipt of the packs. After these were completed and when SPPs were introduced in 1982 and 1983, BPL continued to receive both 5-litre and single packs. Whilst Annual Reports suggest SPP use did contribute to increasing plasma supply it is not possible to quantify this. The introduction of SAG-M in 1984 and the need for a new pack to accommodate a larger volume of plasma thereafter eclipsed the role played by the SPP in supplying plasma to BPL.

Billie Tomlinson, Inquiry Legal Team

Matthew Hill, Counsel to the Inquiry

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