INFECTED BLOOD INQUIRY

Dr Richard Lane, Director of BPL: Presentation

Introduction

1. Dr Richard Lane was the Director of the Blood Products Laboratory ("BPL") from September 1978 to 1990. With the assistance of the CBLA's legal team, an extensive Proof of Evidence was drafted as part of his contribution to the HIV Haemophilia Litigation. It outlined his historical actions and views with regards to a number of topics, including self-sufficiency, the hepatitis risk and the AIDS risk.

2. There were six drafts of the Proof, but the most full and complete draft is the 5th draft, dated 10 December 1990.[1] This is the draft on which the Inquiry has relied as the basis for this presentation. It is made clear when information is gathered from somewhere other than the 5th Draft of the Proof of Evidence. The 6th Proof is dated 11 December 1990.[2]

3. It must be borne in mind that the drafts are all unsigned and were not finalised, presumably because the litigation settled and a final draft was therefore never required. It is important also to bear in mind the context in which the drafts were prepared: namely on behalf of the CBLA with a view to defending the CBLA's actions and decisions in the litigation. To a significant extent the 5th Proof contains comments and opinions on the allegations made by the Plaintiffs in the litigation and on particular documents; with regard to the latter, it is not known how the document selection was made or by whom.

4. This presentation is not intended as a detailed overview of Dr Lane's work; rather the aim is to assist Core Participants in understanding what Dr Lane's position and views were as at 1990. This presentation thus follows the thematic and chronological order laid out in the 5th Draft. Evidence is drawn from a number of documents, most of which were also referenced in the Proof. More generally, the key documents and events relating to BPL will be explored as part of other presentations during the Inquiry's March 2022 hearings.

[1] Dr Lane, Proof of Evidence, 5th Draft, 10 December 1990, CBLA0000005_002
[2] Dr Lane, Proof of Evidence, 6th Draft, 11 December 1990, CBLA0000034_002

Dr Lane's Proof of Evidence

Brief Overview of Dr Lane's Career

5. Prior to his Directorship at BPL, Dr Lane held various positions in paediatrics, medicine and surgery, and became Senior House Officer in Pathology at the West Middlesex Hospital in 1961.[3]

6. Between 1962 and 1966 Dr Lane was a research fellow in Haematology in the Department of Pathology, Royal Maternity and Samaritan Hospitals in Glasgow; and between 1966 and 1973, he was employed as a Scientific Officer at the Medical Research Council Experimental Haematology Unit at St Mary's Hospital Medical School in London.[4]

7. From 1969 to 1970, he spent time as the Senior Fellow of Medicine in the Department of Haematology and Medicine at the University of Washington, Seattle, and at King County Central Blood Bank in Seattle, USA.[5]

8. Between 1973 and 1975 Dr Lane was a lecturer in Haematology at St George's Hospital, London, and then between 1975 and the date he took up his post as Director-designate at BPL, Dr Lane was a Consultant Haematologist to the North East Thames Regional Blood Transfusion Centre in Brentwood, Essex.[6]

[3] CBLA0000005_002, pg. 1-2, [2]
[4] CBLA0000005_002, pg. 1-2, [2]
[5] CBLA0000005_002, pg. 1-2, [2]
[6] CBLA0000005_002, pg. 1-2, [2]

9. Dr Lane was appointed Director-Designate of BPL in April 1977 and became Director in September 1978.[7] In his capacity as Director, Dr Lane was responsible for the day-to-day management of BPL, as well as the Plasma Fractionation Laboratory ("PFL").[8]

10. Dr Lane also belonged to the World Health Organisation Expert Advisory Panel on human blood products and related substances as well as to the International Society of Blood Transfusion.[9]

11. Dr Lane was a member of the Department of Health Advisory Group on Hepatitis and its Working Party on Anti-D, the Department of Health Advisory Committee on the Viral Safety of Blood and was a founding member of the British Blood Transfusion Society.[10]

[7] CBLA0000034_002, pg.1, [1]
[8] CBLA0000005_002, pg.1, [1]
[9] CBLA0000005_002, pg.2, [3]
[10] CBLA0000005_002, pg.2, [3]

Self-sufficiency and the Blood Transfusion Service

Overview

12. Dr Lane characterised the argument advanced by the Plaintiffs in the HIV litigation as: *"had England and Wales been self-sufficient in factor VIII concentrate, fewer haemophiliacs would have required imported commercial factor VIII concentrate which carried a higher risk of contamination with HIV."*[11] His opinion was that this contention was *"probably correct"* based on data which suggested that, pro rata, there was a lower incidence of HIV infection in haemophilia sufferers treated with BPL/PFL produced concentrates compared with those treated with US commercial concentrates.[12]

13. However, due to the length of time it would have taken to achieve self-sufficiency, he believed that "*any decision to pursue self-sufficiency as a goal, could only have been taken at a time when HIV was unknown and, therefore, on the basis that self-sufficiency was not just desirable but necessary for some other reason."*[13] He rejected the argument that hepatitis presented such a reason, as *"hepatitis is very different indeed in terms of risk when compared with HIV."*[14] This opinion was later expanded on in the "Hepatitis" section of the Proof.

14. Dr Lane considered that *"in the 1970s, self-sufficiency was considered desirable but it was not seen as an imperative in that external alternative sources of supply were available."*[15]

15. He also stated that he did not hold the CBLA responsible for the inability to deliver self-sufficiency as, *"in common with their predecessors in managing BPL/PFL, they did not*

[11] CBLA0000005_002, pg.21, [59]
[12] CBLA0000005_002, pg.21, [61]
[13] CBLA0000005_002, pg.22, [62]
[14] CBLA0000005_002, pg.22, [62]
[15] CBLA0000005_002, pg.23, [63]

control the Transfusion Service and, more importantly, the funds necessary to substantially increase production."[16]

16. In essence, Dr Lane's opinion was that *"to aim for self-sufficiency with a view to achieving it before the emergence of HIV would have to have involved taking a decision to do so (and starting to implement this) by the mid 1970s"*, but that this was unachievable due to the *"inability on the part of all those concerned to make any accurate assessment of what "self-sufficiency" really equated to and a complete lack of any knowledge of HIV or the risk it was to present some 8 years later."*[17]

1973 to 1977

17. Dr Lane did not become Director-Designate of BPL until April 1977, and therefore his overview of the period 1973 to 1977 was not first-hand. He believed that at the start of the 1970s, *"self-sufficiency was seen as desirable but not immediately essential"*, and *"a number of major obstacles lay in the path of the pursuit of this objective"*.[18] In his opinion these obstacles were:

a. The lack of proper financial coordination to implement policies covering the activities of Regional Transfusion Centres, BPL/PFL and Haemophilia Centres;[19]

b. The fact that NHS funding from the Department of Health and Social Security ("DHSS") was distributed through the Regional Health Authorities, which were *"to all intents and purposes responsible for allocation of budgets, and the DOH would not intervene in the exercise of their discretion."* There was *"no discernible benefit, demonstrable in cost savings"* to Regional Health

[16] CBLA0000005_002, pg.23, [65]
[17] CBLA0000005_002, pg.24, [68]
[18] CBLA0000005_002, pg.27, [73]
[19] CBLA0000005_002, pg.27, [74]

Authorities in investing in their Transfusion Centres to increase FFP production.[20]

18. Dr Lane wrote that part of the problem was that, at the time, no one knew what self-sufficiency would or should look like: "*What was "self-sufficiency"? The reality proved difficult to forecast. The problem lay in estimating the future requirements of the increasing haemophiliac population for factor VIII.*"[21] Judging the requirements became more difficult with the move from cryoprecipitate to concentrate during the 1970s. At the start of the 1970s, cryoprecipitate was used to treat severe haemophilia patients in the majority of cases, but by the end of the decade, "*most if not all severe haemophiliacs were using factor VIII concentrate, which completely eclipsed cryoprecipitate as the treatment of choice*".[22] As a consequence, *"estimates of factor VIII use were constantly increasing"*.[23]

19. A further problem in Dr Lane's opinion was that key players involved in the process defined self-sufficiently differently.[24] He characterised the definition of self-sufficiency followed by Dr Maycock and some members of the DHSS as: "*the amount of plasma and concentrate produced from it which was needed to treat haemophiliacs in the way they were treated using cryoprecipitate.*"[25] Others, clinicians in particular, felt that self-sufficiency was determined by the *"amount wanted by their patients to lead as near normal a life as possible."* Dr Lane argued that *"estimates arrived at on either basis were, as we now know, wrong."*[26]

1974

[20] CBLA0000005_002, pg.27, [75]
[21] CBLA0000005_002, pg.28, [79]
[22] CBLA0000005_002, pg.28-29, [79]
[23] CBLA0000005_002, pg.29, [80]
[24] CBLA0000005_002, pg.30, [84]
[25] CBLA0000005_002, pg.30, [84]
[26] CBLA0000005_002, pg.30, [84]

20. According to Dr Lane, 1974 was a year *"taken up with discussions about the need to increase the production of factor VIII"*. It was the year that the Health Minister Dr David Owen became involved, though *"not much was achieved."*[27]

21. To meet the increasing demand, more plasma needed to be fractionated but Dr Lane stated that they did not have the facilities to fractionate additional plasma if collected. [28] Dr Lane made clear his belief that *"funds were required for investment in a new fractionation plant and this required a policy decision by the DOH."*[29]

1975

22. At the start of 1975, Dr Owen set aside £500,000 of government funds to increase the production of factor VIII. The stated intention of the Minister for the money was *"to make the United Kingdom self-sufficient in two or three years"*, though for Dr Lane it was clear that *"a one-off payment with a view to producing factor VIII from some 275,000 donations was clearly not sufficient, without continuing investment, to increase the production of factor VIII beyond this figure."*[30]

23. On 17 March 1975, Mr Brandes (DHSS, HS2) wrote a memo to Mr Alexander at the DHSS, discussing Lord Owen's self-sufficiency programme and describing the effort required of Regional Transfusion Directors (RTDs), *"some of whom may not see eye to eye with their clinical colleagues treating haemophilia."*[31] It was said that some Haemophilia Centre Directors envisaged home prophylaxis, whereas others were not fully persuaded of its practicability and value.

24. Dr Lane believed that this memo gave *"some clue to the mismatch between the "target" of producing factor VIII from 275,000 donations and what was actually required."*

[27] CBLA0000005_002, pg.33, [89]
[28] CBLA0000005_002, pg.34-35, [92]
[29] CBLA0000005_002, pg.34-35, [92]
[30] CBLA0000005_002, pg.38, [99]
[31] Memo from L. H. Brandes to Mr Alexander, 17 March 1975, CBLA0000260, pg.2 [4]

[32] It supported his belief that Dr Maycock and the DHSS *"were concentrating on what was believed to be the appropriate level of production to treat patients when a bleed occurred"*, ignoring any allowance for home prophylaxis.[33] For Dr Lane, not including factor VIII for home prophylaxis in target estimates *"may in part explain some of the discrepancies between what BPL actually resolved to produce (and could reconcile with their capacity) and what others estimated was actually needed."*[34]

25. Dr Lane also noted the significance of the reference to factor VIII yield being 30-40% at paragraph 5 of the memo.[35] He called this *"frankly absurd even at the time this memorandum was produced."* with yields at the time in the region of 20%[36] He wrote that he was *"somewhat puzzled as to why figures which were obviously very optimistic were not challenged by Dr Maycock at the time, since he obviously received a copy of the memorandum and his manuscript note gives no indication of disagreement with this part of the text."*[37]

1976

26. Dr Lane described the distribution of blood products up to December 1976 as "*somewhat ad hoc*".[38] Upon reviewing the documentation, he noted a great deal of correspondence from clinicians on behalf of individual patients seeking supplies directly from BPL, and seemingly no formalised procedure for the distribution of concentrates, and in particular none which would encourage RTCs to increase their supply of FFP to BPL.[39]

27. From 1 December 1976 onwards, NHS factor VIII was delivered to the RTCs in an amount proportional to the number of patients treated at the Haemophilia Centres of that

[32] CBLA0000005_002, pg.40, [104]
[33] CBLA0000005_002, pg.40, [104]
[34] CBLA0000005_002, pg.40, [104]
[35] CBLA0000005_002, pg.40, [104]
[36] CBLA0000005_002, pg.40, [104]
[37] CBLA0000005_002, pg.40, [104]
[38] CBLA0000005_002, pg.40, [104]
[39] CBLA0000005_002, pg.40, [104]

region in 1974.[40] It was agreed that patients allergic to cryoprecipitate or already on home treatment with NHS concentrate should be given priority.[41]

28. Dr Lane described this scheme of distribution as a prelude to the 'pro-rata' arrangement, which he was instrumental in introducing after becoming Director of BPL.[42] Under the scheme, RTCs had factor VIII returned to them in quantities that were pro-rata to their contribution of FFP to BPL for fractionation.[43] At this point, Dr Lane believed that RTCs started to see *"reward for their individual efforts in increasing the supply of FFP"* and this had the subsequent effect of *"increasing the supply of FFP and the drive towards self-sufficiency."*[44]

29. On 11 March 1976, a meeting was held at the DHSS to discuss factor VIII production, at which Dr Watt of PFC Scotland suggested that Edinburgh's yield was between 30-35% and they aimed to reach 70% yield.[45] Dr Lane described the figure of 30-35% as "*much higher than I would have expected was possible at the time",* and the figure of 70% as "*frankly ludicrous".*[46] Dr Lane also expressed suspicion at Dr Watt's costing of Scottish product at 4.2p per iu against NHS product estimated at 6p per iu.[47]

30. In July 1976, Dr Maycock wrote a paper entitled "*The Preparation of factor VIII to provide 35m. iu per year*".[48] It revised earlier calculations for the number of donations and volume of plasma required to produce 35m iu of factor VIII. Dr Lane described these figures as "*rather more satisfactory than some of those appearing in Dr Maycock's earlier calculations, although a 30% yield which he assumes is still, in my view, too high. 20% would have been closer to the real yield."*[49]

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[40] CBLA0000005_002, pg.40, [104]
[41] CBLA0000005_002, pg.40, [104]
[42] CBLA0000005_002, pg.45, [115]
[43] CBLA0000005_002, pg.45, [115]
[44] CBLA0000005_002, pg.45, [115]
[45] Minutes of a meeting held at DHSS, 11 March 1976, CBLA0000343, pg.3, [4]
[46] CBLA0000005_002, pg.47, [119]
[47] CBLA0000005_002, pg.47, [119]
[48] Paper, "The Preparation of Factor VIII to provide 35m. iu per year", July 1976, CBLA0000402
[49] CBLA0000005_002, pg.47-48, [120]

31. On 3 August 1976, Mr Dutton (DHSS, HS2A) wrote a memo to Dr Waiter which stated that the Expert Group on the Treatment of Haemophiliacs thought that factor VIII requirements would continue to rise until over 40m iu were being administered per annum. [50] It was estimated that by mid-1977, between 31m and 34m iu per year would be supplied by the NHS, of which 12m to 15m iu would be in the form of concentrate in England and Wales. Dr Lane viewed this estimate as fairly accurate of the then prevailing position, although he argued that Mr Dutton *"seems to ignore the fact that cryoprecipitate was ceasing to be the treatment of choice."*[51]

32. In October Dr Maycock produced a handwritten note entitled "*Sheffield 22/10/76*".[52] It included a sketch of a graph, which Dr Lane argued suggested that Dr Maycock believed *"that the demand would flatten out quite considerably, notwithstanding the extraordinary steep climb to the level of consumption as it then stood."*[53] In Dr Lane's opinion, *"this was unfortunately entirely bogus"*, and in his view *"there were no grounds for believing that the demand would follow the pattern shown on the graph."*[54]

33. For Dr Lane, 1976 was summarised as a year:

> *"...dominated by the continuing cryoprecipitate debate, the implementation of increases in production facilitated by the £500,000 injection of finance, and debate about the "target" necessary to achieve self-sufficiency and the confusion sown in all this by "targets" which related to capacity to produce rather than volume necessary to achieve self-sufficiency and to what was <u>needed</u> rather than what the patients and clinicians <u>wanted</u>...The mismatch between what was being achieved (with a struggle), what was required to meet the current self-sufficiency requirements in concentrate and what, had anyone looked beyond current usage, would be necessary to achieve self-sufficiency for the future was all too obvious."*[55]

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[50] Memo from T. E. Dutton to Dr Waiter, 3 August 1976, CBLA0000408, pg.1, [1]
[51] CBLA0000005_002, pg.49-50, [124]
[52] Handwritten note by Dr Maycock re: Sheffield, 22 October 1976, CBLA0000474, pg.2
[53] CBLA0000005_002, pg.51, [128]
[54] CBLA0000005_002, pg.51, [128]
[55] CBLA0000005_002, pg.52, [131]

34. He argued that *"decisive action would have been required (backed by considerable funding) to plan a facility which would be ready by the end of the decade, and of a size which would leapfrog sufficiently far ahead to cater for the burgeoning demand for factor VIII concentrate."*[56]

1977

35. On 15 April 1977, Dr Lane became the Director-Designate of BPL. However, he felt that Dr Maycock kept him *"very much in the background."*[57] Dr Maycock continued to attend Transfusion Director meetings as representative of BPL without Dr Lane, and although Dr Lane was given work planning the 'Stop Gap' proposals to upgrade BPL facilities, it was not until Dr Maycock retired that he found he was *"able to exert much influence or control over BPL/PFL."*[58]

36. At a Haemophilia Centre Directors' meeting held on 13 January 1977, Dr Macdonald from the Royal Infirmary in Glasgow stated that if Liberton received £25,000 for new capital equipment and money for extra running costs, including a 24 hour shift system, they would have the capacity to make 60m iu of factor VIII per year.[59] Dr Lane described this figure as *"nonsense"* and expressed surprise to find that it was not apparently challenged in the meeting if the minutes were correct.[60] He stated his belief that a disproportionate amount of money was spent on the SNBTS; he notes that in 1975/6, £15.8m was spent on the NBTS in England and Wales for a population of 49 million, compared with expenditure of £3.5m in Scotland for a population of 5.5 million.[61]

37. In September 1977, Dr Lane contributed to a report on BPL for the Advisory Sub-Committee on Blood Products and Blood Group Reference Laboratories of the Central

[56] CBLA0000005_002, pg.53, [131]
[57] CBLA0000005_002, pg.53, [132]
[58] CBLA0000005_002, pg.53, [132]
[59] Minutes of the meeting of Haemophilia Centre Directors of the UK, 13 January 1977, PRSE0002268, pg.16
[60] CBLA0000005_002, pg.55, [137]
[61] CBLA0000005_002, pg.58, [144]

Committee for the National Blood Transfusion Service.[62] Appendix A1 outlined the changes Dr Lane wanted to make concerning the method of sending FFP to BPL and the preparation of factor VIII. It focused on changing from 5 litre bags of pooled plasma (made up of plasma from 20-30 donations) to single donation packs. He argued that 5 litre pooling operated an 'open' system involving greater workload, more equipment and a greater risk of contamination than a 'closed' system of plasma collection using single packs. He believed this would boost the supply of plasma for fractionation and resolve the difficulties associated with testing pooled plasma for HBV.

38. In the above paper, Dr Lane concluded that although critics would argue the cost would be large, given that considerable sums had to be spent rebuilding BPL, it would be wrong to *"limit the potential of this investment by the installation of old technology"*[63] He listed the ways in which he thought the shortage of finance could be mitigated:

a. *"by integrated policy within the NBTS (i.e. Regional Centres and BPL) to avoid reduplication of expenditure;*

b. *"improving yield within BPL;*

c. *"changing the Department's attitude to free-spending on expensive commercial imported alternatives to the NBTS – produced therapeutic fractions and serological reagents;*

d. *"adhering to the Department of Health's principle that the Health Service shall make all possible attempts to become self-sufficient."*[64]

39. Dr Lane also proposed introducing charges for NBTS products as he thought it *"would result in more effective use and lessen the problem of non-administration of the*

[62] Report to the Advisory Sub-Committee on Blood Products and Blood Group Reference Laboratories of the CCNBTS, September 1977, CBLA0000664
[63] CBLA0000664, pg. 11-12
[64] CBLA0000664, pg. 11-12

product."[65] However, he wrote that he believed *"Dr Maycock would in no way have supported this contention."*[66]

40. Describing a meeting between BPL and the DHSS held on 25 October 1977, Dr Lane wrote that the Department made it *"quite clear that no commitment could be made at that stage to any specific solution."*[67] At the meeting, Dr Lane had set out the three main problems he felt were facing the push to self-sufficiency:

a. the continuing pressure to produce more factor VIII with BPL having almost reached the limit of its present production capacity;

b. the implications of the recommendations of the "Trends" Working Group which pointed to substantial expansion of production of factor VIII and albumin over the next 5 to 10 years; and

c. the application of the Medicines Act to the NBTS and the probability that a number of processing units in RTCs and in BPL itself would not meet the standards being demanded by the Medicines Inspectorate, particularly in relation to open systems for handling blood and plasma.[68]

1978

41. The closure of the Lister Institute was announced on 17 April 1978.[69] Dr Lane wrote a report, addressed to Professor Mollison, for the Management Sub-Committee, where he described its closure as a *"unique opportunity for the development and future of BPL"* as it presented a chance to *"buy all or part of the Lister site to facilitate the development of*

[65] CBLA0000005_002, pg. 63-64, [158]
[66] CBLA0000005_002, pg. 63-64, [158]
[67] CBLA0000005_002, pg. 65, [160], referring to a note of a meeting held on 25 October 1977 at the BPL, CBLA0000682
[68] Note of a meeting held on 25 October 1977 at the BPL, CBLA0000682, pg.1, [3]
[69] CBLA0000005_002, pg.70, [170]

BPL".[70] He raised the question of the replacement governing body and stressed that any managing committee should remain small and distinct. He also noted his belief that *"development of BPL is hampered predominantly by the inordinately slow process of decision-taking by DHSS."* In retrospect, Dr Lane considered that the closure of the Lister Institute *"could not have come at a better time"* and the Department decided to buy the Lister site, keep staff and obtain temporary management arrangements.[71]

42. In addition to the introduction of single plasma packs and pro rata arrangements, Dr Lane described three opportunities for increasing FFP that arose during the period relevant to the HIV litigation:[72]

i. Lord Owen's £500,000 special allocation, which enabled BPL to effectively double its production of factor VIII from 5m iu to 11m iu per annum;

ii. The development of optimal additive solutions which resulted in an increase of 30% recovered plasma volume from each donation; and

iii. The potential to increase use of plasmapheresis, which would have enabled donors to donate a greater plasma volume.[73]

43. In Dr Lane's view, the problem with BPL was that its basic infrastructure had *"remained one which was appropriate to a laboratory engaging in research and relatively small-scale production."*[74] The buildings dated back to the 1950s and were not fit for purpose as they were *"old, small and not appropriately designed for manufacturing."* Despite these shortcomings, the facility was making a significant contribution to the production of factor VIII.

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[70] Report to Professor Mollison, Closure of the Vaccines and Sera Laboratories of the Lister Institute, Elstree and the Implications for the Blood Products Laboratory, 21 April 1978, CBLA0000758, pg.3 [1]
[71] CBLA0000005_002, pg.70-71, [171]
[72] CBLA0000005_002, pg.72, [174]
[73] CBLA0000005_002, pg.72, [174]
[74] CBLA0000005_002, pg.74, [180]

44. At a meeting of the North East Thames Region Working Party in Haemophilia on 29 November 1978, the minutes recorded that Dr Lane stated that they needed a facility which could produce at least 110m units of factor VIII per annum, and £15m was needed in the short-term to upgrade BPL.[75]

1979

45. In Dr Lane's opinion, *"in terms of self-sufficiency, by 1979 it was too late, (having regard to the four to five years it would take to plan and build a new facility), for a decision in this regard to have made any difference if, as I would submit, the majority of severe haemophiliacs were infected with HIV before 1985."*[76]

46. In May 1979, Dr Lane authored a paper entitled "*The Function of Stop-Gap and Phased Redevelopment of the Blood Products Laboratory*" in which he considered factor VIII demand.[77] He calculated the total use of factor VIII in 1977 as 48.5m iu and compared this against the Trends Working Party level of 60m iu for use by the mid-1980s.[78] Considered in this way, it was clear that *"factor VIII use was therefore in a period of rapid growth."* due to gradually increasing numbers of haemophilia patients diagnosed and treated, and expected increase in lifespan with associated increased incidents of illness and surgery, as well as a move towards home therapy and prophylactic care.[79] In the longer term, he advocated for a serious appraisal of plasmapheresis, and in the short term a move to a pro-rata arrangement with RTCs.[80]

47. In April 1979, BPL was visited by the Medicines Inspectorate. Dr Lane's *"expectation that they would be severely critical of the facility was confirmed by their*

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[75] Minutes of a Meeting of the Haematology Working Party North East Thames Region, 29 November 1978, CBLA0000877, pg. 3; see also a different version of the minutes at BART0000686
[76] CBLA0000005_002, pg.79, [187]
[77] Dr Lane, Report on "The function of stop-gap and phased redevelopment of the Blood Products Laboratory", 31 May 1979, BPLL0001508
[78] CBLA0000005_002, pg.79-80, [189]
[79] CBLA0000005_002, pg.79-80, [189]
[80] CBLA0000005_002, pg.80, [190]

comments."[81] Indeed, Dr Lane had been so convinced of the outcome that he wrote a letter to Mr Dutton of the DHSS setting out his observations of their visit prior to the publication of their first report.[82] He wrote:

> *"Mindful of the shortcomings of the existing system and somewhat contrary to the previous Director's feelings, I both welcome and encourage this inspection, since I believe it is quite contrary to good manufacturing practice to use a privileged situation to hide the considerable deficiencies of BPL. In addition and also contrary to the previous Director's views, I believe that Medicines Division, through their Inspectorate and acting on behalf of the Secretary of State for the Health Service, have a responsibility to assist a Central Health Service Production Laboratory like BPL to carry out its function in the best possible way."*[83]

48. In the letter, Dr Lane laid out the three main problems facing BPL:

> *"First, intrinsic deficiencies of the building and the constraints arising primarily out of the leasehold arrangements which govern BPL's development; second a quantitative and qualitative deficiency in staff arising from our inability to compete with industry at the level required to recruit process/technical and scientific staff which are needed; third, the fact that the laboratory is in a transitional stage between what Malcolm Harris chose to call, quite aptly, a "cottage industry" into a major production process moulded along commercial industrial lines. During this transition, the entire approach of staff to process and to environmental care has to be altered."*[84]

49. In May 1979, Dr Lane revised his earlier paper "*The Function of Stop-Gap and Phased Redevelopment of the Blood Products Laboratory*" to collect together thoughts and plans starting with Stop-Gap and, building on this, the proposals for a phased

[81] CBLA0000005_002, pg.93, [193]
[82] Letter from Dr Lane to Mr Dutton, 2 May 1979, CBLA0000938
[83] CBLA0000938, pg.1, [2]
[84] CBLA0000938, pg.2, [1]

redevelopment.[85] As BPL was to be redeveloped, he increased factor VIII production targets to 12m iu per annum.[86] In retrospect, he explained this revision was "*trying to avoid what seemed to have been the pattern in the past of always aiming for the lowest current usage as a target with the inevitable consequences, and instead to aim sufficiently ahead of current usage to be more certain of hitting the target when an enlarged facility was commissioned.*"[87]

50. At a Joint Management Committee (JMC) meeting on 13 June 1979, Dr Lane commented on what he believed the findings of the Medicines Inspectors would be.[88] The meeting recorded argued that, "w*hile the possibility had to be faced that there might be no money available to make any radical changes at BPL for perhaps 3 or 4 years, everything possible had to be done to improve the state of affairs from within whatever money was available.*" He also "*urged the Department, in any submission made to Ministers, to emphasise that BPL was a money saving unit. The value of the products which it could turn out, given the necessary facilities, was equal to the whole of the current NBTS budget.*"

51. On 8 August 1979, Dr Lane wrote to Dr Holgate at the DHSS, , detailing his concerns following the recent visit of the Inspectors.[89] He drew his attention to the fact that following the inspection, the DHSS had temporarily stopped the 'Stop-Gap' programme, since the implementation of the Inspectorate's recommendations had to be within the cash limit of the year's budget. He was concerned that the DHSS appeared not to take the point that the 'Stop-Gap' programme would superimpose what he believed would be many of the important recommendations and requirements of the Inspectorate, and wanted some of the work to be initiated before the end of the financial year. Dr Lane also wrote that he believed these interruptions eroded his authority as he had responsibility for product safety and quality control. He wrote:

[85] CBLA0000005_002, pg.82, [196]
[86] CBLA0000005_002, pg.82-83, [198]
[87] CBLA0000005_002, pg.82-83, [198]
[88] Minutes of a meeting of the Joint Management Committee, 13 June 1979, BPLL0008488, pg.2-3, [4]
[89] Letter from Dr Lane to Dr J. A. Holgate, 8 August 1979, CBLA0000967

"Particularly, this is irksome when the interruptions have their basis in the political manoeuvrings of DHSS and the new government. We appear to be playing two games that have got inextricably combined, one deals with blood products and product safety, and the other deals with the administrative organisation of the Health Service. I can only record how dangerous I feel this confusion is and how it weakens the authority of my directorship."[90]

52. Dr Holgate replied on 14 August 1979.[91] He sympathised and agreed with the two exercises having been mixed up. He assured Dr Lane that they were all on the *"same wavelength"*, and that the formal discussions of the reports and the forwarding of the final recommendations had been accelerated, and they were in broad agreement that developing all aspects of the 'Stop-Gap' programme *"which will achieve improved quality <u>without</u> impairing the use of the premises for those purposes suitable in conjunction with a completely new premises"* was how to proceed. The Medicines Inspectors' report arrived at BPL on 13 August 1979, although Dr Lane was absent at that time.[92]

53. On 10 September 1979, Mr Firstbrook wrote a letter to Mr Harley enclosing the conclusions and recommendations of the Medicines Division.[93] The seventh conclusion was: *"if this were a commercial operation we would have no hesitation in recommending that manufacture should cease until the facility was upgraded to a minimum acceptable level."* However, the eight conclusion was that production at Elstree could continue *"as blood products are essential to the health and wellbeing of the nation and as alternative sources of supply are severely restricted."* In his Proof, Dr Lane noted that strictly speaking, this was not correct, as many products could have been purchased from commercial sources which were not severely restricted.[94] However, he stated that as deficient as the facility was, some aspects compared favourably with some facilities that were licensed in the USA.

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[90] CBLA0000967
[91] Letter from Dr Holgate to Dr Lane, 14 August 1979, CBLA0000977
[92] CBLA0000005_002, pg.89, [214]
[93] Letter from Mr Firstbrook (Medicines Division) to Mr Harley (DHSS), 10 September 1979, CBLA0000988
[94] CBLA0000005_002, pg. 90-91 [218]

54. At a JMC meeting on 12 September 1979, there was reference to the concern which he was expressing at the time about his liability as Director of BPL under the Medicines Act if an adverse event was caused by a BPL product.[95] Dr Lane recalled that despite the matter being referred to DHSS solicitors and despite taking his own advice from the solicitors for North West Thames RHA on the issue, no one could give him a clear answer as to the extent of his responsibilities.[96]

55. On 12 September 1979, Mr Dutton wrote to Dr Lane to propose the establishment of a Working Group to prepare a paper for the JMC on the implementation of the Medicines Inspector's recommendations.[97] Dr Lane replied on 13 September, objecting to the limited terms of reference of the Working Group and its composition, and strongly urged that "*a more definitive and far-reaching study of the problem*" was undertaken.[98] In his Proof, Dr Lane explained that he had in mind *"keeping Stop-Gap and the phased redevelopment of BPL alive – not just a make-do and mend to the Medicines Inspectors' report."*[99] He thought it essential that the Working Group include the Consultant Advisor to the DHSS, someone to represent RTCs' interests, and someone to represent the Scientific and Technical Committee. These requests were turned down, which Mr Dutton explained was partly in the interest of speed but also because of limited funds.[100]

56. Dr Lane formally responded to the Medicines Inspectors' report in a letter of 14 September 1979 addressed to Mr Flint.[101] He indicated that he accepted their report in general terms.

57. On 19 September 1979, Dr Lane prepared a report entitled *"Future Preparation of Plasma Protein Fractions by NBTS: A reassessment of requirements"*.[102] The paper

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[95] Minutes of the 4th meeting of the Joint Committee for the Central Blood Laboratories, 12 September 1979, CBLA0000992, pg.6, [6]
[96] CBLA0000005_002, pg.91-92, [220]
[97] CBLA0000005_002, pg.92, [221]; CBLA0000993.
[98] Letter from Dr Lane to Mr Dutton, 13 September 1979, CBLA0000994, pg.1
[99] CBLA0000005_002, pg.92, [221]
[100] Letter from Mr Dutton to Dr Lane, 25 September 1979, CBLA0001001
[101] Letter from Dr Lane to Mr Flint, 14 September 1979, CBLA0000995
[102] Dr Lane, "Future Preparation Plasma Protein Fractions by NBTS: A reassessment of requirements", 19 September 1979, CBLA0000998, pg.7

proposed a Special Health Authority be set up, and advocated for a co-ordinated joint approach based on the essential relationship between raw material supply and manufacture, and noted that *"at no time has there been an integrated administration capable of executive co-ordination of the NBTS programme."* Dr Lane explained that this paper was prompted by the need to ensure any attempt to resolve the problems facing BPL took into account the problems facing RTCs who provided the raw materials.[103]

58. At an ad hoc Regional Transfusion Directors meeting on 26 September 1979, it was noted that there was not universal acceptance of the idea that blood products should be distributed by BPL to RTCs proportionately to plasma supplied by them (although the minutes recorded that a distribution scheme on this basis would prove generally acceptable with some safeguards for regions with special problems).[104] Dr Lane wrote that he viewed this as *"hardly surprising, since there were some Regions and Centres providing very little plasma when compared to others."*[105] The minutes noted that there was a tendency to revert back to cryoprecipitate in some regions, in part due to a shortage of money to collect more plasma for BPL or buy commercial concentrate.

59. The Scientific and Technical Committee also met on 26 September.[106] At the meeting, Mr Harley from the DHSS said that for the time being, proposals for expenditure would have to be limited to the amount already budgeted for the 'Stop-Gap' programme, and there was no certainty additional money could be found. Dr Lane said the money currently available to finance "Stop-Gap" would do little more than to pay for improved cleanliness which was the first priority.

60. In October 1979, Professor Mollison drafted a memo commenting on the implications of an adverse report on BPL for the NBTS.[107] One point he made was that plasma from some paid donors was known to be more likely to transmit disease,

[103] CBLA0000005_002, pg.93, [223]
[104] Minutes of a meeting of an ad hoc group of RTDs, 26 September 1979, DHSC0002195_044, pg.1
[105] CBLA0000005_002, pg.94, [225]
[106] Minutes of the third meeting of the Scientific and Technical Committee for the Central Blood Laboratories, 26 September 1979, CBLA0001005 , pg.2
[107] Memo on the implications for the NBTS of an adverse report on the BPL by the Inspectors of Medicines Division, October 1979, DHSC0002195_069

particularly hepatitis, than plasma from volunteer donors. Dr Lane asserted that this was, in his opinion, *"an oversimplification and probably not correct so far as hepatitis NANB is concerned"*, although *"it was most probably true of HIV."*[108]

61. At an ad hoc meeting of RTDs in Sheffield on 11 December 1979, Dr Lane emphasised, in the context of a discussion about a pro-rata system, that it was essential to build a contractual relationship into any future system, including a binding commitment on any RTC which undertook to supply plasma to BPL; supplies were tending to fall off and there would almost certainly be a drop in the quantity of blood products available unless the DHSS took drastic action.[109] He also invited members to consider the practicability of rationalising plasma production, possibly by concentrating production in 4 or 5 centres with extensive use of plasmapheresis. Members pointed out that this was only feasible if money was provided, and Dr Lane suggested the expense could be included in the BPL budget.

1980

62. The Scientific and Technical Committee met on 23 January 1980.[110] At the meeting, Mr Harley explained that Ministers had decided to defer the eventual decision on building a new laboratory within the NHS until the other possibilities had been investigated, one of which was offering BPL to the private sector. Dr Lane pointed out *"the need to ensure that the Minister [Dr Gerrard Vaughan] had fully appreciated the inter-dependence between the laboratory and the Regional Transfusion Centres."*[111] The minutes noted that Dr Lane *"urged that consideration of the phased redevelopment of BPL should continue and not be deferred pending discussion with industry."* In his Proof, Dr Lane wrote that he found the meeting disappointing.[112]

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[108] CBLA0000005_002, pg.96-97, [230-231]
[109] Note of an ad hoc meeting of RTDs, 11 December 1979, CBLA0001035. Although this is said to be an ad hoc meeting of RTDs, the note records those present as being only Dr Tovey, Dr Bird, Dr Gunson, Dr Lane, Dr Walford and Mr Dutton.
[110] Minutes of a meeting of the Scientific and Technical Committee for the Central Blood Laboratories, 23 January 1980, CBLA0001052
[111] CBLA0001052, pg. 2
[112] CBLA0000005_002, pg.99, [239]

63. At a JMC meeting on 20 February 1980, it was announced that the Department anticipated around £750,000 would be available for capital development at BPL in 1980/81, and Dr Lane had been authorised to proceed with 'Stop-Gap' and several other projects.[113] Dr Lane replied that he was worried that the total cost of even the relatively short-term redevelopment of the laboratory would cost possibly as much as £2m to £2.5m over 2-3 years. He pointed out that this money would go a considerable way towards the construction costs of a new laboratory. The Committee agreed that redevelopment would need to be closely monitored by a project committee, to be chaired by Dr Walford.

64. Dr Gerrard Vaughan (Minister of State for Health) visited BPL on 21 March 1980.[114] Dr Lane wrote that his impression of the visit was that, having heard the reservations of staff and management about BPL being commercially run, the Minister "*was convinced of the need to upgrade BPL in the short term and redevelop it thereafter.*" However, Dr Lane was dismayed to find that the Minister later "*decided to reduce available funds which were already inadequate for the task of satisfactorily upgrading BPL in the short term, on the understanding that a decision would be taken about long term redevelopment.*"[115]

65. Dr Lane described the meeting of the Scientific and Technical Committee on 23 April 1980 as containing a "*bombshell*".[116] Dr Harris (DHSS) was minuted as saying:

> "*Ministers recognised that there were difficulties at BPL which needed to be resolved and they and the Department would accept responsibility for these deficiencies. However, Medicines Divisions' requirements for improvements had to be considered in the light of the present financial situation, and the Department had accordingly agreed a package of measures which had been approved by the STC. Ministers were now asking that these measures be re-examined to see if there might be scope for further savings. Ministers were anxious that the Public Accounts Committee should be satisfied that the cost of the short-term*

[113] Minutes of the 6th meeting of the Joint Management Committee for the Central Blood Laboratories, 20 February 1980, CBLA0001068, pg. 3
[114] CBLA0000005_002, pg.103, [252]
[115] CBLA0000005_002, pg.103, [252]
[116] CBLA0000005_002, pg.105, [253]

improvement at BPL was justified in view of the fact that the Laboratory was to be rebuilt. Dr Harris agreed that the requirements of the Medicines Act could not be fully met except by complete rebuilding, but Ministers had nevertheless decided that BPL should continue to make blood products."[117]

66. Dr Lane wrote that the implications were clear; they had been promised a sum of money which was inadequate to meet the *"very modest targets"* of 'Stop-Gap', but now it seemed that even this sum was to be reduced.[118] Without the money needed, 'Stop-Gap' as originally envisaged, which took care of most of the Inspectors' concerns, could not be pursued, and future manufacturing requirements would be further compromised. In Dr Lane's view, *"insufficient money was being spent even by way of temporary expedient to ensure the standards were improved sufficiently to satisfy the Medicines Inspectorate's immediate requirements, much less achieve the aims and objects of the original Stop-Gap proposals."*[119]

67. On 1 May 1980, Dr Lane wrote to Dr Harris, expressing his concern at the recent meeting and asking that his letter be shared with the Minister since *"it is clear that following his visit to the Laboratory there are misunderstandings about the interim requirements."*[120] Whilst he agreed that a decision to build a new laboratory at the earliest opportunity could lead to considerable capital savings, *"this was not to say that the Laboratory can be run in the intervening years without adequate financial support."* The existing building would need to function for at least another five years, and deficiencies had to be rectified. He noted that the deficit in factor VIII and albumin production represented an annual loss to the NHS of £5.5m given the cost of commercial product. BPL had not grown since 1977 but clinical demand was projected to double in the five-year period from 1977. Unless BPL met the additional yield, the cost of imported products would be in excess of £30m. He concluded that:

[117] Minutes of the 5th Meeting of the Scientific and Technical Committee, 23 April 1980, CBLA0001093, pg. 3
[118] CBLA0000005_002, pg.105, [254] [255]
[119] CBLA0000005_002, pg.106, [257]
[120] Letter from Dr Lane to. Dr Harris (DHSS), 1 May 1980, CBLA0001099

"Manufacturing requirements at BPL during this interim period must be decoupled from considerations relating to a new laboratory. BPL will need to continue to work at a stated output with maximum safety and cost effectiveness up to the day it is closed prior to handover to new premises. The Laboratory's requirements are dependent upon its production targets and not the reverse. A controlled expansion means limited budgetary increases but the Laboratory pays for itself at present and there is no reason why, with proper management, it should not continue to do so during this interim period."[121]

68. Dr Lane wrote to Mr Harley on 22 May 1980, enclosing a revised budget for 'Stop-Gap'.[122] In his Proof, he explained that the budget had been changed *"to keep to the Minister's imperative that expenditure should be limited to matters of absolute necessity."*[123] The new version of 'Stop-Gap' was redesignated as MARP01 - "Medicines Act Rehabilitation Programme".

69. At a meeting at the DHSS on 11 June 1980, Dr Lane was asked to provide a list of what he would wish to spend money on if only £500,000 capital was available in 1980/81. [124] He agreed to consider, but advised very strongly against such a course, and "*could accept no responsibility for the outcome of this level of expenditure since it would lead to loss of key staff and eventually to major loss of productive capacity."* In his Proof, he likened the situation to one "*where you are told you may purchase a motor car and subsequently informed that you only be allowed a sum of money which is materially less than the purchase price and should decide which bits of the car you would like to buy."*[125]

70. The revised budget which Dr Lane produced (approximately £813,000) was considered at a meeting of the Scientific and Technical Committee on 18 June 1980.[126] Dr

[121] CBLA0001099, pg. 2-3
[122] Letter from Dr Lane to Mr Harley, 22 May 1980, CBLA0001107
[123] CBLA0000005_002, pg.108-109, [261]
[124] Note of a meeting to discuss expenditure on the upgrading of BPL, 11 June 1980, CBLA0001112, pg.1
[125] CBLA0000005_002, pg.109, [263]
[126] Minutes of the 6th meeting of the Scientific and Technical Committee, 18 June 1980, CBLA0001119, pg. 2-3

Lane argued that his revised budget was the basic minimum if safety and production were to be increased and the Chairman felt that the Committee should support the revised budget.

71. At a meeting of the Finance Sub-Committee of the JMC on 13 August 1980, it was confirmed that Ministers had agreed to capital expenditure of £1.3m for short-term improvements at BPL over the financial years of 1980/81 and 1981/2, and additional revenue of £100,000 from 1981/82, mainly for increased staffing.[127] Dr Lane commented that he would be recruiting senior staff "*once the future of the laboratory became clearer*". In his Proof, he expanded upon his view that the uncertainty regarding its redevelopment was bound to harm recruitment.[128]

72. On 16 September 1980 Dr Lane prepared a report for the Plasma Fractionation Working Party, which concluded that there would be a shortage of plasma for the new production facility, which had a production capacity that would require the supply 410,000 litres of FFP. He anticipated a considerable deficit in terms of supply.[129] Dr Lane looked at the alternatives means of obtaining plasma: importing USA paid-donor plasma taken by plasmapheresis, plasmapheresis of volunteer donors within NBTS, or the introduction of SOG-SAG suspended red cells, which would only be a partial solution.

73. Mr Harley wrote to Dr Lane on 22 December 1980, enclosing two further reports which the Medicines Inspectors had made.[130] In the second report written by John Ayling, Principal Inspector, it was stated that "*the management of this Centre is very obviously not providing the proper control systems.*" and only with proper management could adequate systems of control be implemented.[131] Dr Lane reflected that this was true, and observed that the public sector terms and conditions were insufficient to attract suitably qualified staff.[132]

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[127] Note of a meeting of the Finance Sub-Committee of the JMC, 13 August 1980, DHSC0001883
[128] CBLA0000005_002, pg.113, [276]
[129] Report by Dr Lane for the Plasma Fractionation Working Party, 16 September 1980, CBLA0001153
[130] Letter from Mr Harley to Dr Lane enclosing reports, 22 December 1980, CBLA0001221
[131] CBLA0001221, pg. 10-11
[132] CBLA0000005_002, pg.118-119, [288]

1981

74. In a letter published in The Times on 2 January 1981 Mr Meakin of the University of Bath wrote suggesting that the insufficiency of blood products in the United Kingdom was *"largely self-imposed by bureaucracy"*.[133] He wrote that production in England and Wales was outmoded and inefficient whereas production in Scotland was limited by blood supply and the Edinburgh plant was seriously underutilised.

75. In Dr Lane's opinion, the reality was that PFC's capacity as shown in a later trial at PFC was not matched by similar capacity of preceding and following steps in the manufacturing process, and the question of 24 hour shift working remained unresolved.[134] He also believed that in the period between 1981 to 1985, *"there was no major imbalance between plasma supply and BPL/PFL's ability to fractionate plasma produced in England and Wales."*[135] In fact, he said, there was no material surplus of plasma which was being wasted and thus no immediate role for PFC to play.

76. On 4 February 1981 Dr Lane produced a paper in which he described the interim programme as *"an intensely uncomfortable period for the Laboratory in which the strains are applied in all directions."*[136]

77. Dr Lane wrote to Dr Harris on 9 March 1981, advocating for central control and management of the Transfusion Service and the establishment of a Special Health Authority. [137] He concluded, *"If this government continues to support self-sufficiency in blood and blood products for the UK, then presumably it will not nullify the major financial investment by disregarding the co-existent requirement for competent management."*

[133] Brian Meakin, University of Bath, Letters in the Times, "Impeding Flow of Blood" and "The flow of Blood", 2 January 1981, CBLA0001236
[134] CBLA0000005_002, pg.121-122, [292]
[135] CBLA0000005_002, pg.122, [293]
[136] Dr Lane, "Blood Products Laboratory: Summary of Performance in September 1979", 4 February 1981, CBLA0001258, pg.4
[137] Letter from Dr Lane to Dr Harris, 9 March 1981, CBLA0001307

78. On 16 June 1981, Dr Lane wrote to Dr Gunson, observing that plasma collected by plasmapheresis in the USA could be purchased if in the future not enough plasma was collected to supply the redeveloped BPL's increased capacity.[138] He noted that the risks of using US plasma inherent in the plasma and in the final product to the same extent, but that it would be argued that *"control over fractionation in the UK would provide a better measure of assurance than by leaving fractionation to US laboratories."*

1982

79. On 8 January 1982, Dr Lane wrote to Dr Harris, advising him that the combined BPL and PFL production had increased in 1981 and that the combined output of Factor VIII for 1982 was 22m iu.[139] He wrote that this increase was *"most commendable"* given the difficult year with interim building programmes and the application of the Medicines Inspectorate requirements.

80. Dr Lane published BPL/PFL's Annual Report for 1981/82 on 20 April 1982.[140] He wrote that input of FFP to BPL had increased for the first time in five years and BPL was now approaching capacity or above capacity, but the *"major design faults of BPL...continue to exert a real compromising effect on laboratory performance and product safety."*[141]

81. On 13 May 1982, Dr Lane wrote to RTDs alerting them to a restriction on the supply of factor VIII for about three months or four months, starting in June 1982.[142] The intention was to catch up once laboratory facilities were restored to fully-commissioned working, with no overall loss of factor VIII over the period.

82. In July 1982, the Policy Steering Group produced an appraisal of various redevelopment options.[143] The document recommended that the option which satisfied

[138] Letter from Dr Lane to Dr Gunson, 16 June 1981, CBLA0001383
[139] Letter from Dr Lane to Dr Harris, 8 January 1982, BPLL0011369
[140] Dr Lane, Annual Report 1981/2, 20 April 1982, CBLA0001570
[141] CBLA0001570, pg. 1
[142] Letter from Dr Lane to all RTDs, England and Wales, 13 May 1982, CBLA0001579
[143] "An Appraisal of Re-development Options for the Blood Products Laboratory", July 1982, CBLA0001606

demand at the lowest cost was a laboratory with a 400 tonne capacity.[144] This was estimated to cost £21.1m spread over the years 1982 to 1986.[145]

1983

83. On 17 January 1983, Dr Lane wrote to Dr Wagstaff, Director of the Sheffield RTC, expressing concern following criticism levelled at BPL in minutes of the Blood Preservation Working Party[146] which had been circulated at the 187th RTD meeting on 14 January 1983, which he described as unfounded.[147]

84. Dr Lane countered criticism of BPL by providing figures which, he said, confirmed that BPL had managed to substantially increase factor VIII productivity. In his Proof, Dr Lane described how the document also contained inaccurate yield figures and expressed frustration that the Working Party continued to advocate for the use of 5 litre packs, despite Dr Lane's efforts in explaining the logic of single donation packs.[148]

85. On 25 May 1983, Dr Lane prepared a document which provided a graphic analysis of the redeveloped BPL's capacity and projected plasma demand, with an anticipated capacity to fractionate 450 tonnes of FFP per annum from December 1985.[149] He described this document as part of his efforts *"to encourage increases in FFP production in anticipation of the new BPL facility"*.[150]

86. At the 8th meeting of the Advisory Committee on the NBTS ("ACNBTS"), held on 17 October 1983, Dr Lane reported that *"the CBLA had mounted a campaign to make RHAs fully aware of the role of BPL and the long-term benefits to Authorities of immediate investment in plasma procurement."*[151] The meeting agreed that the DHSS should discuss with the CBLA what assistance might be given by the Department on this matter. In his

[144] CBLA0001606, pg. 11
[145] CBLA0001606, pg. 14
[146] Minutes of the 187th RTD Meeting, 14 January 1983, CBLA0001663, pg. 4
[147] Letter from Dr Lane to Dr Wagstaff (Sheffield RTC), 17 January 1983, CBLA0001664
[148] CBLA0000005_002, pg.155, [368]
[149] Dr Lane, "PESC Estimates related to BPL Manufacturing Requirements", 25 May 1983, CBLA0001708
[150] CBLA0000005_002, pg.155-156, [369],
[151] Minutes of the 8th Meeting of the ACNBTS, 17 October 1983, CBLA0001763, pg. 4

Proof, Dr Lane noted that this assistance was never given.[152] He also remarked that supply of FFP to BPL for the first six months of 1983 amounted to 73,704kg, which actually showed a *"reasonable increase"*.

87. Dr Lane prepared two papers in 1983 *"which were designed to try and increase awareness of the need to improve the supply of FFP."*[153] "Plasma Supply - National Blood Transfusion Service"[154] was intended to bring together information on BPL's likely future capacity and requirements for plasma to inform RTDs, and it was discussed at the 188th RTD meeting on 18th May 1983.[155] The paper anticipated that a combination of recovered plasma, SAG-M plasma and plasmapheresis would be necessary to reach BPL's future capacity.

88. The second paper focused on the value of SAG-M, and its implications for plasma procurement.[156] It estimated that with the addition of SAG-M, around 290 ml of plasma could be removed per donation, an increase of around 35.5% from the routine 190 ml removed from a unit of red cell concentrates in 1983. However, Dr Lane also predicted problems of clinical acceptance.

1984

89. On 16 January 1984, Dr Lane wrote a report which stated that factor VIII output at BPL had increased to 30m iu per annum, and RTCs had doubled their input of FFP to 150,000kg.[157] He reported that site works for the new production building had commenced in April 1983 and were expected to cost in excess of £21m.

90. Dr Lane wrote that by the end of 1984, it was clear that *"implementation of self-sufficiency would be affected by the requirements of maintaining product safety."*[158]

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[152] CBLA0000005_002, pg.156, [370]
[153] CBLA0000005_002, pg.158, [375]
[154] CBLA0001778
[155] CBLA0000005_002, pg.158, [375], Minutes of the 188th RTD Meeting, 18 May 1983, CBLA0001707, pg 2
[156] The value of SAG-M systems in the provision of plasma products, Dr Lane, January 1983, CBLA0001779
[157] Dr Lane, BPL Report April 1982 - April 1983, April 1983 - December 1983, 16 January 1984, DHSC0002239_003, p. 3
[158] CBLA0000005_002, pg.163-164, [389]

Whilst he was planning for a facility which, at the time, was believed would achieve self-sufficiency when it was commissioned, and working towards increases in FFP supply, the implementation of heat treatment meant that there were losses of product, and during the initial stages of the production of 8Y, there was *"a drop in yield which had implications for the supply of factor VIII."*[159]

1985

91. Dr Lane believed that by the start of 1985, *"self-sufficiency was beginning to drop away as an issue."*, pointing to the absence of questions regarding plasma supply and self-sufficiency in RTD meeting agendas.[160]

92. In July 1985, Dr Lane prepared a paper evaluating the MARP01 project.[161] It calculated that the final cost of the project was £3,038,000, but product produced by the investment was estimated to be valued at £12,257,000, so the project had effectively paid for itself.

93. At the 11th meeting of the ACNBTS on 6 November 1985 Dr Lane expressed concern about maintaining a quarantine supply of plasma.[162] The minutes note *"It was agreed that the DHSS would continue to monitor the conversion of Regions' firm promises into action plans for plasma production."* In his Proof, Dr Lane noted that this indicated *"DOH were playing a rather more direct role than historically had been the case in encouraging increases in supply to keep BPL functioning."*[163]

Summary of Self-Sufficiency Claims

94. In response to an allegation that CBLA failed to set in place a proper policy of development and improvement after its creation in December 1982, Dr Lane stated: *"the*

[159] CBLA0000005_002, pg.163-164, [389]
[160] CBLA0000005_002, pg.165, [392]
[161] Dr Lane, "Evaluation of the MARP 01 Programme and Other Capital Expenditure Projects Between 1981 and 1983", 24 July 1985, CBLA0002223
[162] Minutes of the 11th Meeting of the ACNBTS, 6 November 1985, CBLA0002277, pg. 2
[163] CBLA0000005_002, pg.167, [397]

redevelopment of BPL as originally planned would have resulted in the new facility being commissioned by December 1985 at the earliest", which would have been "*too late for it to have had any beneficial effect, so far as the risk of HIV infection in haemophiliacs were concerned".*[164]

95. He conceded that there were some delays and cost escalation in relation to the new BPL facility but asserted that a detailed review of the history of the BPL redevelopment would *"reveal there was no negligence on the part of the CBLA in relation to their involvement in the project."*[165] It is, of course, relevant to note that this Proof was being given on behalf of the CBLA, Dr Lane's then employers, which had only been responsible for the operation and management of BPL and PFL since 1 December 1982.

96. Dr Lane's understanding was that throughout the period, BPL was generally ahead of the supply of FFP in terms of capacity to fractionate.[166] Despite the *"obvious constraint"* that BPL had no control over RTCs or the funding they received, he wrote that they did their best to encourage RTCs to maximise their contributions of FFP, in particular through:[167]

a. introducing a pro-rata system of distributing factor VIII which rewarded increases in FFP production;

b. encouraging the change from 5 litre bags to single plasma packs;

c. encouraging clinicians to use concentrated red cells;

d. promoting more extensive use of plasmapheresis;

e. encouraging the wider use of SAG-M; and

[164] CBLA0000005_002, pg.168, [402]
[165] CBLA0000005_002, pg.168, [402]
[166] CBLA0000005_002, pg.168, [402]
[167] CBLA0000005_002, pg.168, [402]

f. introducing a highly effective test for the hepatitis screening of donors.[168]

97. In response to an allegation that there was a failure to cooperate with RHAs sufficiently, Dr Lane believes that from 1978 onwards, *"our"* involvement in efforts to encourage RTCs to increase supply of FFP was extensive.[169] *"We advised the DOH, Regional Transfusion Centre Directors and (as appropriate), Haemophilia Centre Directors as to what BPL would require by way of FPP supplies, and how we thought the required increases could be achieved."*[170]

98. He emphasised that they could not *"force Regional Health Authorities to implement our recommendations and the DOH showed their procedural reluctance to intervene and direct that Regional Health Authorities allocate a certain proportion of their funds on specified Transfusion Centre activities."*[171]

99. In response to an allegation that there was a failure, from 1982, to assess future needs for factor VIII, Dr Lane argued that by the time CBLA was established, the future needs of factor VIII had been accurately estimated.[172] In response to an allegation that, from 1982, they failed to achieve targets, Dr Lane wrote that he believed that due to the financial and regulatory constraints imposed by the DHSS and the Medicines Inspectorate, the target of 30m iu of factor VII was "*the best that could be set",* and this was achieved.[173]

100. In response to an allegation that there was a failure to use the spare production capacity in Scotland, Dr Lane stated that, in his mind, the belief that there was any significant spare capacity at PFC Liberton was *"a myth".*[174]

101. In response to an allegation that there was a failure to achieve self-sufficiency by 1989, Dr Lane wrote that self-sufficiency "*ceased to be relevant by the end of 1985 when*

[168] CBLA0000005_002, pg.168, [402]
[169] CBLA0000005_002, pg.170, [403]
[170] CBLA0000005_002, pg.170, [403]
[171] CBLA0000005_002, pg.170, [403]
[172] CBLA0000005_002, pg.171-172, [404]
[173] CBLA0000005_002, pg.172, [406]
[174] CBLA0000005_002, pg.172-173, [407]

heat treated products (NHS and commercial) made from tested plasma, were available in quantities sufficient to satisfy haemophilia patients' requirements for treatment."[175]

[175] CBLA0000005_002, pg.174, [410]

Hepatitis Risk and/or Risk of Other Viral Infection

Overview

102. Dr Lane wrote that hepatitis B (HBV) *"proved fatal in relatively few cases and was an ever reducing risk through the 1970s."*[176] He asserted that although HBV and Non A Non B hepatitis were universally recognised during the 1970s, the steady significant increase in patient demand for factors VIII and IX indicated that the benefit exceeded the *"perceived risk or discomfort from hepatitis infection."*[177]

103. By 1980, through the use of factor VIII and factor IX, haemophilia patients *"could look forward to normalisation of their lives in terms of usefulness, quality and longevity."*[178] However, HIV *"dramatically changed the balance: the product which saved life, itself assumed the trappings of a death sentence. An invidious choice."*[179]

Hepatitis B and Hepatitis Non-A Non-B: 1973 - 1985

1973

104. In 1973, Dr Biggs wrote a report entitled *"Jaundice and Antibodies directed against factors VIII and IX in patients treated for Haemophilia or Christmas Disease in the United Kingdom"*, which Dr Lane described as an early seminal work.[180] Dr Lane asserted, however, that one had to be particularly careful about the implications to be drawn from the report, as it was published too early to provide a foundation for reliable conclusions with regard to the transmission of HBV through factor VIII concentrate.[181] The results were based on jaundice, which was not reliable in estimating the actual incidence of HBV or

[176] CBLA0000005_002, pg.183, [435]
[177] CBLA0000005_002, pg.183, [435]
[178] CBLA0000005_002, pg.183, [435]
[179] CBLA0000005_002, pg.183, [435]
[180] Dr Rosemary Biggs, "Jaundice and Antibodies directed against factors VIII and IX in patients treated for Haemophilia or Christmas Disease in the United Kingdom", 5 September 1973, HCDO0000581; CBLA0000005_002, pg.184, [436]
[181] CBLA0000005_002, pg.184, [436]

non-A non B hepatitis (NANBH).[182] He pointed out that Dr Biggs wrote that the use of freeze dried concentrate did not cause a dangerous increase in episodes of jaundice compared to cryoprecipitate, but at the time, concentrate usage was at a low level.[183]

1974

105. Dr Lane noted that a *"strong impression"* emerged over the next few years that US commercial concentrates were less safe than their NHS counterparts, but *"this was incorrect so far as the incidence of transmission of Non-A Non-B hepatitis was concerned."* [184] Screening for the Hepatitis B antigen was routinely used both in the US and the UK and so by 1980, clinicians were, he said, only really concerned with NANBH.

1975

106. In September 1975, Dr Craske alongside Dr Kirk wrote some proposals for a prospective study on the relationship of HSsAb test results in haemophilia patients with the risk of contracting HBV after infusion with the factor VIII concentrate Hemofil.[185] Three hypotheses were put forward to explain the finding that there continued to be a substantial failure to prevent post-transfusion hepatitis: testing methods were not sensitive enough; other known viral agents were responsible; or other, as yet unknown viruses, caused a significant amount of post-transfusion hepatitis.[186] Dr Lane observed that *"the first and third possibilities were indeed, we now know, correct."*[187]

1976

[182] CBLA0000005_002, pg.184, [437]
[183] CBLA0000005_002, pg.184, [437]
[184] CBLA0000005_002, pg.186-187, [443]
[185] Prospective Study of the relationship of BHsAB test results in Haemophiliacs to the risk of contracting Hepatitis B after transfusion of factor VIII concentrate, September 1975, CBLA0000311
[186] CBLA0000005_002, pg.190, [449]
[187] CBLA0000005_002, pg.190, [449]

107. In December 1976, Dr Smith (PFL) wrote a report comparing cryoprecipitate with intermediate purity concentrate.[188] It stated that *"cryoprecipitate cannot compete with concentrate in safety, reliability, or convenience for the patient, and claims that it is cheaper or more economical of plasma resources have doubtful validity."*[189] In Dr Lane's view, the paper was *"a clear statement of common sense backed up by fact."*[190] He contended that *"there was no doubt that, for the majority of clinicians and patients, concentrates were the treatment of choice and consumption of the commercial products was growing rapidly."*[191]

1977

108. Dr Craske published a survey called "*Haemophilia Associated Hepatitis - 1974-75 in the United Kingdom a Retrospective Study*" in which he studied two types of hepatitis - HBV and a short incubation Non-B hepatitis.[192] He found that there was an overall incidence of 17.7% post-transfusion hepatitis with Hemofil, whereas there had been a reported incidence of 1.8% prior to the introduction of commercial concentrate.[193] The survey impressed Dr Lane, who describes it as "*something of a state of the art document at that time.*"[194] Although the survey did not extend to include NHS factor VIII, Dr Lane believed that the work supported what he believed was in fact the case, namely that US commercial concentrate was more likely to be infected with HBV, having regard to the fact that plasma was obtained from paid donors.[195]

109. In September 1977, Dr Lane wrote a Report for the Advisory Sub-Committee covering the year ending July 1977.[196] In Appendix A1, he suggested that RIA screening for

[188] Dr Smith, "Comparison of cryoprecipitate and intermediate purity concentrate for the treatment of haemophilia", December 1976, CBLA0000534
[189] CBLA0000534, pg. 1
[190] CBLA0000005_002, pg.192-193, [453]
[191] CBLA0000005_002, pg.193, [454]
[192] J. Craske, "Commercial factor VIII associated hepatitis, 1974-75, in the United Kingdom: a retrospective survey", 5 September 1977, HSOC0000009
[193] HSOC0000009, pg. 8-9
[194] CBLA0000005_002, pg.194, [456]
[195] CBLA0000005_002, pg.198-199, [465]
[196] Dr Lane, Report on the BPL and Blood Group Reference Laboratory, September 1977, CBLA0000664

HBsAg of all donor units in RTCs should be promoted.[197] He noted that RIA testing at source "*would provide the greatest clinical benefit to potential recipients*". Testing 5 litre pools unnecessarily implicated 25-30 other donations, and additional positive results would be found if testing at source. This formed part of the reason that Dr Lane advocated a move to single donation packs.[198]

1978

110. In January 1978 Dr Lane wrote a paper entitled *"Stop-Gap provision for plasma fractionation at BPL"* in which he noted that control of HBsAG transmission depended upon constant surveillance of whole human plasma so that antigen-positive material could be excluded from processing.[199] Even the most sensitive RIA tests did not exclude the possibility of hepatitis transmission, but provided "*the highest level of confidence currently available in the safety of a plasma fraction.*" His paper noted that there was a problem with large plasma pools, and strict control on plasma pool size was "*a compromise between the increasing risk in large pools and the efficiency of the fractionation process.*"[200] He advocated for the extension of RIA testing to RTCs, to ensure HBsAg was excluded from large plasma pools. To reduce costs, he suggested a more economic RIA test could be developed in collaboration with BPL, RTC Edgware and the Middlesex Hospital Virology Department, as opposed to using a commercial test.

111. At a meeting with the DHSS on 18 January 1978, Dr Lane reported commercially produced RIA tests cost between 30p and 90p, depending on the volume of testing performed.[201] By contrast, it was hoped that the RIA test developed between BPL, the Middlesex Hospital and the North London RTC would cost between 10p and 15p per test.[202] In response to the suggestion that this would lead to some units being tested twice by the same method at additional cost, Dr Lane stressed that "*he could not accept any testing over*

[197] CBLA0000664, pg. 32
[198] CBLA0000005_002, pg.200, [469]
[199] Letter from Dr Lane to Professor Mollison, enclosing report, "Stop-Gap Provision for Plasma Fractionation at BPL", 28 July 1978, CBLA0000801, pg. 2
[200] CBLA0000801, pg. 3
[201] Note of a Discussion on RIA Testing at the BPL held at DHSS, 18 January 1978, CBLA0000715
[202] CBLA0000005_002, pg.203-204, [475]

which he did not have direct control" in order to achieve maximum safety standards at BPL.

112. When summarising 1978, Dr Lane wrote that in the absence of established evidence that NHS factor VIII transmitted HCV, *"the logical drive was to increase output of NHS factor VIII from UK plasma since this appeared to carry less risk and to make sure that hepatitis B testing efficiency was optimised in the NBTS."*[203]

1979

113. Dr Lane suggested that the most interesting document produced during the year was the 1979 report of the Haemophilia Centre Directors' Hepatitis Working Party.[204] This stated that the prevalence of hepatitis in 1978 and 1979 was around the same level as that observed in 1976-7 but there had been an increase in the proportion of NANBH reported in patients with mild coagulation defects receiving concentrate for the first time to cover operations.[205]

1980

114. Dr Lane wrote to Mr Brechin (DHSS) on 7 January 1980, providing a full costing of the RIA test kits compared with commercial tests.[206] In his Proof, Dr Lane noted that at the time, BPL and PFL were using their own RIA test, but most RTCs were still using the reverse passive haemagglutination (RPH) test.[207]

115. At the fourth meeting of the Scientific and Technical Committee on 23 January 1980, Dr Lane outlined his proposals to make BPL's RIA test "*available to the Health Service at a cost very substantially below that which Centres were currently paying"* and the meeting agreed that the switch to RIA was desirable. Members recommended that the

[203] CBLA0000005_002, pg.207, [482]
[204] CBLA0000005_002, pg.208-209, [486]
[205] HCDO0000135_023.
[206] Letter from Dr Lane to Mr Brechin (DHSS), 7 January 1980, CBLA0001045
[207] CBLA0000005_002, pg.210, [493]

Department should consider all possible means of funding this project, and if necessary, invite Regions to pay for it.[208]

116. Up until this point, BPL had been represented by Dr Drummond-Ellis on the Haemophilia Centre Directors' Hepatitis Working Party.[209] On 1 April 1980 Dr Lane wrote to Dr Craske to say he would like to represent BPL personally since hepatitis was "*clearly going to be a major problem area for some years to come.*"[210] Dr Craske confirmed that he could join the Working Party on 22 April.[211]

117. On 29 September 1980, Dr Lane sent a memo to Dr Smith on the topic of pool sizes, indicating that he could, "*see no reason why the limit on donations per patch should not be lifted, enabling us to process 900 - 1,000kg of some plasmas on some days. In connection with the risk of transmission of hepatitis, I am sure that once one has exceeded the 100 - 200 kg pool-size, one has already exceeded any possibility of small pool protection.*"[212] He noted that he had spoken to Dr Craske who agreed on this point.

118. In his Proof, Dr Lane set out his view as to why large pools were preferable to small ones:[213]

i. economy of scale;

ii. very small pools did not provide enough product to treat severe haemophiliacs, who would require product from another pool, thereby defeating the object of a small pool approach;

[208] Minutes of the 4th Meeting of the Scientific and Technical Committee, 23 January 1980, CBLA0001052
[209] CBLA0000005_002, pg.212, [499]
[210] Letter from Dr Lane to Dr Craske, 1 April 1980, CBLA0001089
[211] CBLA0000005_002, pg.212, [499]
[212] Memo from Dr Lane to Dr Smith, 29 September 1980, CBLA0001173
[213] CBLA0000005_002, pg.219, [512]

iii. 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*"; and

iv. large pools produced a more standardised and predictable product in terms of quality.[214]

1981

119. In the minutes of the second meeting of the ACNBTS, held on 23 February 1981, it was noted that members felt it was wrong to levy a charge of 20p for BPL's RIA test when the actual cost could be less and it would pose an additional financial burden on RTCs.[215] The Chairman, Dr Harris, explained that the Department's experts had advised that the price of the test should be comparable with equivalent commercial tests. In his Proof, Dr Lane described the delay in the introduction of the BPL RIA test at RTCs as caused by "*non-essential commercial considerations*".[216]

120. On 27 February 1981 Dr Lane prepared a proposal on the development of factor concentrates with reduced risk of hepatitis transmission.[217] It stated that *"the significance of a product demonstrably free of hepatitis risk cannot be ignored and it is essential that BPL/PFL be well placed to take advantage of such developments."* He pointed out that owing to the risk of handling large quantities of plasma known to be infective, the work would have to be sited outside the regular production area. In his Proof, Dr Lane noted he was alluding to the use of the old Lister laboratories if converted for research and development.[218] It was agreed that he should formally forward his proposals with likely costs, with a view to the DHSS approaching the office of the Chief Scientist to consider funding.

[214] CBLA0000005_002, pg.219, [512]
[215] Minutes of the 2nd meeting of the ACNBTS, 23 February 1981, CBLA0001287, pg. 5
[216] CBLA0000005_002, pg.225, [525]
[217] "The development of methods for the production of coagulation factor concentrates with reduced risk of hepatitis transmission", 27 February 1981, CBLA0001291
[218] CBLA0000005_002, pg.227, [529]

121. In March an article by Dr Lane was published in the journal of Medical Laboratory Sciences entitled "Hepatitis B surface antigen testing: The Blood Products Laboratory Radioimmunoassay (BPL/RIA) system".[219] In his Proof, he explained that the purpose of the article was to bring attention to the fact that BPL had developed an inexpensive RIA kit which had a sensitivity at least equal to that of the best commercial preparations.[220] The article stated that, "*the pooling of plasma has always caused concern at the BPL since a single plasma donation negative by HA at the 20 ng/ml level would probably be missed by RIA when pooled with 25 other donations. Without doubt HBsAg has been missed in the past for this reason, and positive donations incorporated into pools for fractionation.*"[221]

1982

122. In the Annual Report covering 1981/2 dated 20th April 1982 Dr Lane noted that RIA HBsAg tests developed by BPL had been produced and supplied to all UK Transfusion Centres and some PHLS laboratories, with limited exceptions.[222] At BPL, 35,711 routine tests for HBsAg had been carried out, with 16 positive results. 14 positive samples had come from plasmas supplied in 5 litre bags, and Dr Lane noted "*the changeover to single donor packs with individual pack testing at the RTC's will provide greater security against this happening in the future.*"

123. At a meeting of the Haemophilia Centre Directors' Hepatitis Working Party on 13 September 1982, Dr Craske described a study underway at Oxford.[223] He informed the meeting that nine out of nine patients treated with one batch of concentrate developed NANBH from commercial and NHS factor VIII. Dr Lane observed in his statement that this study was "*the foundation for the conclusion (later confirmed) that US and UK factor VIII and factor IX concentrates were equally infective so far as hepatitis Non-A Non-B was*

[219] Dr Lane, "Hepatitis B surface antigen testing: the Blood Products Laboratory radioimmunoassay (BPL/RIA) system, 2 March 1981, CBLA0001310
[220] CBLA0000005_002, pg.228, [531]
[221] CBLA0001310, pg. 1
[222] Dr Lane, Annual Report 1981/2, 20 April 1982, CBLA0001570, pg. 5
[223] Minutes of the 10th Meeting of the UK Haemophilia Centre Directors Hepatitis Working Party, 13 September 1982, HCDO0000556

concerned, the only variation between the two being that NHS concentrates resulted in mainly asymptomatic infection."[224]

1983

124. In his Proof, Dr Lane described how, in 1983, the issue of how to deal with NANBH in their products *"merged with the HIV issue giving impetus to both ourselves and commercial fractionators in connection with research into virus inactivation."*[225]

125. In July 1983 Dr Lane wrote *"AIDS, progress with heat treatment of human plasma products"*.[226] The paper suggested that the severity of NANBH had "*motivated plasma fractionation organisations to re-examine means whereby hepatitis virus can be inactivated in large-pool concentrates."*

126. In his Proof, Dr Lane pointed to a report of the Hepatitis Working Party, presented to the 14th meeting of Haemophilia Centre Directors on 17 October 1983, which suggested that the prospective study at Oxford had showed a 100% risk on first exposure of contracting NANBH, whether NHS or commercial Factor VIII was used.[227]

1984

127. On 8 November 1984, Dr Kernoff sent Dr Lane a paper called *"High risk of Non-A Non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin"*.[228] The paper noted that 9/9 patients treated with USA-derived commercial products and 10/12 treated with NHS products developed acute NANB hepatitis, but hepatitis following commercial products appeared to be more severe.[229]

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[224] CBLA0000005_002, pg.242, [559]
[225] CBLA0000005_002, pg.245, [569]
[226] Dr Lane, "AIDS, progress with heat treatment of human plasma products", 26 July 1983, CBLA0001729
[227] CBLA0000005_002, pg.250, [576].
[228] Letter from Dr Kernoff to Dr Lame, 8 November 1984, CBLA0001917
[229] Kernoff et al, "High risk of non-A non-B hepatitis after a first exposure to volunteer or commercial clotting factor concentrates: effects of prophylactic immune serum globulin", 20 June 1984, PRSE0003439, pg. 1

128. In December 1984, the Lancet published an article "*Blood Transfusion, Haemophilia, and AIDS*".[230] It reported that in the UK, unheated large- pool concentrates prepared from voluntary donors had transmitted NANBH and a first-generation dry heated concentrate had also transmitted the disease.[231] Dr Lane described this as a "*landmark article*".[232]

1985

129. In March 1985, Dr Lane was sent an article written by Dr Combridge and Dr Barbara on the effect of RIA HBsAg screening at English RTCs.[233] The paper showed a fall in HBsAG positive plasma pools detected at the BPL during retesting, which dropped to zero in 1984, after all RTCs and BPL used third generation BPL-RIA tests.[234] In his Proof, Dr Lane claimed that the introduction of third generation RIA tests at BPL in 1979 and the use of second generation tests at RTCs "*largely solved the problem of hepatitis B.*"[235]

Summary of 'Hepatitis' Claims and CBLA's Rebuttal

130. In response to an allegation that the CBLA failed to appreciate sufficiently the risk of infection with hepatitis and the serious and potential fatal nature of hepatitis, Dr Lane emphasised that the CBLA only became responsible for BPL from December 1982, by which time HBV was controlled through RIA testing at BPL, PFL and RTCs.[236]

131. In response to an allegation there was a failure to take sufficient steps to remove or reduce the risk by eliminating the need to use imported commercial factor VIII, heat treating factor VIII and factor IX or reducing pool sizes, Dr Lane referred to the small pool

[230] The Lancet, "Blood Transfusion, Haemophilia, and AIDS", 22 December 1984, CBLA0001964
[231] CBLA0001964, pg. 2
[232] CBLA0000005_002, pg.249, [587]
[233] Letter from Mr Combridge to Dr Lane enclosing paper, B. S. Combridge & J. A. J. Barbara, "Effect of Screening of Serum Donations for HBsAg at English Regional Transfusion Centres by Immunoradiometric Assay", 1 March 1985, CBLA0002077
[234] CBLA0002077, pg. 2
[235] CBLA0000005_002, pg.252, [593]
[236] CBLA0000005_002, pg.254, [597]

experiments undertaken at Oxford, which, he said, *"demonstrated that small pool concentrates offered only limited assurance of safety from transmission of NANB hepatitis."* [237] The reality (in his view) was that to achieve self-sufficiency, *"the logistics of small-pool fractionation, the reduction in efficacy of process and of consistency in quality, argued against the small pool approach."*[238] Small pools would also have been quickly exhausted by severe haemophilia patients and given the knowledge of NANBH in the early 1980s, the reorganisation necessary to change to small-pool concentrates was not justified.[239] By the time AIDS had become apparent, most severe haemophilia patients had *"already become infected with HIV in any event and the solution in the form of heat-treated factor VIII and IX was just around the corner."*

[237] CBLA0000005_002, pg.256, [602]
[238] CBLA0000005_002, pg.256, [602]
[239] CBLA0000005_002, pg.256-257, [603]

The AIDS Risk

1982

132. The earliest reference to AIDS in the documents apparently drawn to Dr Lane's attention by the CBLA was in the minutes of the 13th Meeting of the UK Haemophilia Centre Directors and the subsequent Hepatitis Working Party meeting, both on 13 September 1982, which Dr Lane attended.[240] The minutes noted that Dr Craske had been asked to look into a report from the US that the syndrome had appeared in three haemophilia patients and there was a *"remote possibility that commercial blood products had been involved."*

133. At the first meeting of the UK Working Party on Transfusion-Associated Hepatitis on 27 September 1982, it was decided against widening the brief to include other infections, but it was noted that the experience gained in dealing with hepatitis could be applied to other infections, including *"acquired immune deficiencies"*.[241] In his Proof, Dr Lane referred to an article from September 1982 in the Journal of the American Medical Association[242], which he said would have been routinely available to all scientific staff at BPL/PFL.[243] He observed that as at September 1982 there was a growing body of knowledge, little information as to a primary infectious aetiology, but *"an early implication for the blood supply as a source of transmissible infection"*.[244]

134. On 11 November 1982, Dr Craske wrote to Miss Spooner (Oxford Haemophilia Centre), enclosing a paper on AIDS and informing her that the latest information from the CDC in the US was that there were five haemophiliacs identified with the syndrome and the hypothesis being used to explain the cases, which were in areas of the US where the

[240] Minutes of the 13th Meeting of the UK Haemophilia Centre Directors, 13 September 1982, CBLA0001619, pg. 10, Minutes of the 10th Meeting of the UK Haemophilia Centre Directors Hepatitis Working Party, 13 September 1982, HCDO0000556
[241] Minutes of the first Working Party on Transfusion-Associated Hepatitis, 27 September 1982, CBLA0001625
[242] "Acquired immunodeficiency syndrome cause(s) still elusive", September 24, 1982, CBLA0001624.
[243] CBLA0000005>002, pg.268, [613]
[244] CBLA0000005_002, pg.270, [618]

syndrome had not been previously described, was that *"one or two patients in the incubation period of the disease donated plasma which has since been used to prepare factor VIII or IX concentrates."*[245] He concluded that the likelihood was that other cases would be identified amongst severe haemophiliacs, *"though probably at a low prevalence."* Dr Lane described this as *"one of the earliest documents recognising the possible risk of AIDS for haemophiliacs in general, through treatment with Factor VIII"*.[246] Dr Craske wrote to Dr Lane on 22 December 1982 with a copy of a similar paper and of his paper for the MRC Hepatitis Vaccine Group.[247]

1983

135. Dr Lane was in attendance at the meeting of the UK Working Party on Transfusion Associated Hepatitis on 18 January 1983, at which Dr Craske *"summarised the position as it currently stood in relation to AIDS"*.[248] Dr Lane was also present at the Hepatitis Working Party meeting on 19 January 1983 when there was further discussion of AIDS.[249]

136. According to Dr Lane's Proof, the question of AIDS came up for the first time within the CBLA at a meeting (attended by Dr Lane) on 23 March 1983, at which Professor Bloom suggested that the CBLA should discuss AIDS at its next meeting, and Dr Gunson agreed to provide a report to the CBLA in June following the meeting of the Council of Europe's Committee on Blood Transfusion.[250]

137. On 24 March 1983, Dr Lane wrote a memo on AIDS to Mr Mallory of BPL, copying in (amongst others) Dr Smith and Dr Snape.[251] He wrote that Professor Bloom had drawn the attention of the CBLA to the increasing incidence of reported AIDS in the US. He noted that the high mortality in reported causes was the primary factor *"behind what is described as the American over-reaction to the problem"* and the aetiological factor or

[245] Letter from Dr Craske to Miss Spooner, 11 November 1982, HCDO0000557, pg. 1
[246] CBLA0000005_002, pg. 272, [622]
[247] CBLA0001653_001, CBLA0001653_002 and CBLA0001653_003.
[248] CBLA0000005_002, pg. 274, [625]; NHBT0000023_002.
[249] CBLA0000005_002, pg. 274, [626]; HCDO0000558.
[250] CBLA0000005_002, pg. 276, [628]; CBLA0001690.
[251] Memo from Dr Lane to Mr Mallory, 24 March 1983, CBLA0001691

factors remained unknown. Dr Lane believed that patients potentially at risk in the UK, notably haemophiliacs, were "*evidently concerned*" and resistance against the use of imported American imported concentrates was becoming apparent. "*Equally, there is a likelihood that a return to cryoprecipitate as a desirable form of treatment may become irresistible, whether logical or not.*" He added:

> "*It is necessary for this Laboratory to develop a policy, which may only be implemented on a short-term basis, which will allow for the presentation of a large proportion of NHS factor VIII as cryoprecipitate. Staff will be aware that many Regional Transfusion Centres have not made wet cryoprecipitate for some time and would now be both out of practice and in some cases without the facilities to recommence large-scale production. The implications for BPL source material are very real.*
>
> *A meeting involving those circulated with this memorandum should be set up at the earliest convenient opportunity to discuss the strategical alternatives at BPL for manufacturing small pool freeze-dried cryoprecipitate to off-set the requirement for manufacturing at BTS level. Considerable adjustments to resources would be envisaged and taken account of. Equally, a (temporary) fractionation programme commencing with cryoprecipitate supernatant from the BTCs should also be taken into consideration. The implications concerning factor IX production will need to be examined and the potential benefits of pasteurisation of factor IX given some priority.*"[252]

138. In his Proof, Dr Lane explained:

> "*My memorandum was written against the background of an expectation on my part that as concern amongst haemophiliacs with regard to the AIDS risk heightened, there would come, with that concern, the likelihood of a return (albeit on a temporary basis) to the use of cryoprecipitate as a preferred method of*

[252] CBLA0001691

treatment until the cause of AIDS was properly diagnosed and preventative measures put in place. This would clearly have important effects on BPL as far as our source material was concerned, i.e. plasma would be used to manufacture cryoprecipitate at the Regional Transfusion Centres and not sent to us for fractionating. It seemed to me that against this background we needed to be thinking in terms of converting to the production of small pool freeze-dried cryoprecipitate to assist Blood Transfusion Centres where they were out of practice or otherwise ill equipped to revert to cryoprecipitate manufacture. Neither BPL nor PFL had ever produced cryoprecipitate for transfusion. In the event, the anticipated pressure for a switch to the use of cryoprecipitate as a temporary expedient never happened. It was a matter for the haemophilia clinicians (and to an extent the Licensing Authority if it thought US concentrate unsafe) to direct this change."[253]

139. The meeting suggested in that memo took place on 18 April 1983.[254] Dr Lane advised that BPL had to decide now whether to change course if a move away from concentrates was request. The minutes asserted that discussions with Dr Aronstam (Treloars) indicated that the relationship of AIDS to haemophiliacs *"had not been established nor the extent of the risk"*. Dr Snape was reported as remarking that there was little firm knowledge on how effective heat treatment was on NANBH, nor what the effect on yields would be. The minutes noted several comments, which, amongst others, included:

a. *"Is large pool material worse than small pool? - very little evidence in this area."*

b. *"What would be the effect if BPL only able to produce one half of the UK requirement for FVIII, if heat treated yields were much lower than those seen currently for normal material."*[255]

[253] CBLA0000005_002, p.g.278 [632-33]
[254] Notes of a Meeting held on 18 April 1983, BPLL0008758
[255] BPLL0008758, pg. 2

140. The minutes stated that there was a general feeling that a response to a request for BPL to make small pool material or only heat-treated product would be difficult. The UK only used large donor pools, and "*it would be difficult to change the philosophy, once major progress had been achieved in the SAG(M) programme*".[256] However, the meeting agreed that BPL should go for both small panel and heat treated products, with a careful costing exercise needing to be carried out. "*The overriding concern was that in trying to provide full UK demand with a secure product, BPL may end up not being able to supply the demand.*"[257] Dr Lane posed the question whether the current problem posed by AIDS could be used to obtain financial support for more work in this area. The minutes noted that "*the overriding view was one of wait and see*".

141. In his Proof, Dr Lane stated that, *"to an extent, we were obliged to adopt a policy of "wait and see". We needed directions from the haemophilia clinicians and DOH before we could react to produce what was needed."*[258]

142. The policy to "*wait and see*" was adopted in Dr Lane's note on AIDS prepared for the CBLA on 22 April 1983, which reported that progress with AIDS was *"being kept under regular survey"*.[259] Dr Lane wrote that BPL would continue to manufacture factor VIII, but with continued attention to research and development programmes designed to inactivate transmissible viruses by heat pasteurisation and other methods. Further proposals for resources set aside for virus inactivation would be put to the Authority if it was felt that expansion of the programme was needed. He added that, "*the potential of the Laboratory to manufacture small pool freeze-dried cryoprecipitate in significant amounts, as an alternative to large pool intermediate factor VIII concentrate, has been ruled out on logistic production considerations*." Dr Lane also noted that a first *"genuine report"* of AIDS in a haemophiliac could bring about a sudden and significant request for single unit wet cryoprecipitate for a large number of haemophiliacs: *"Whether this demand could be suppressed is unknown, but it would seriously reduce the efficiency of the current plasma procurement programme to satisfy BPL targets for factor VIII concentrate"*.

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[256] BPLL0008758, pg. 2
[257] BPLL0008758, pg. 3
[258] CBLA0000005_002, p.g.280 [637]
[259] Dr Lane, "Acquired Immune Deficiency Syndrome", 22 April 1983, CBLA0001697

143. In his Proof, Dr Lane explained that these "*logistic production considerations*" were related to laboratory equipment.[260] "*Our facilities were geared towards production of concentrates from large pools. A shift to small pool production would have required a monumental turn-around.*"

144. Dr Lane stated in the Proof that BPL never determined the clinical choice of products, so they continued to prepare intermediate purity concentrates of factor VIII and to develop high purity heated concentrate "*in the absence of an alternative directive from either the market or from the DOH and regulatory authority.*"[261]

145. At the first meeting of the CBLA's Central Committee for Research and Development in Blood Transfusion on 21 June 1983, at which Dr Lane was present, the Chairman (Dr Gunson) outlined the problems caused by AIDS, which "*appeared to be transmitted through blood and blood products.*"[262] There was reference to the DHSS circular, but it was acknowledged that this *"relied on the integrity of the donor"*. The consensus of the meeting appeared to be that *"not enough was known about AIDS to enable any decisions to be made"*, save that Drs Lane, Gunson, Fraser and McClelland should arrange for the formation of an ad hoc group to consider the question of whether sufficient research was being done and report back at the next meeting.

146. Referring to this meeting in his Proof, Dr Lane stated that:[263]

> *"During 1983 scientific information gathering and initiation of research was multi-focal within the UK and for the reason that particular areas of the problem emerged through the haemophilia service, the Blood Transfusion Service, fractionation services, hospital clinicians receiving AIDS patients and the*

[260] CBLA0000005_002, p.g.281 [640]
[261] CBLA0000005_002, p.g.283 [645]
[262] Minutes of the 1st Meeting of the CBLA's Central Committee for Research and Development in Blood Transfusion, 21 June 1983, PRSE0002741
[263] CBLA0000005_002, p.g.285 [649]

virological institutes in leading hospitals. Sharing of information and co-ordination occurred automatically since many key individuals occupied positions on more than one group and the role of the DOH and MRC was secured through observers and led ultimately to the MRC taking a lead role in the British response to problems with HIV infection."

147. Dr Lane mentioned in his Proof that by the spring of 1983, the likelihood of a lymphotrophic virus had been identified, which was a "*compelling reason for continuing with our programme of virus inactivation"* which was given "A1" priority.[264] He stated that the programme had "*already been accorded high priority"*.

148. A further memo was prepared by Dr Lane on 26 July 1983 entitled "Aids: Progress with heat treatment of human plasma products". [265] In it, Dr Lane set out his view that AIDS was likely to include in its aetiology transmission of an infective virus.

149. At the fourth meeting of the Working Party on Transfusion Associated Hepatitis, held on 27 September 1983 and attended by Dr Lane, there was discussion of two cases in haemophiliacs in the UK (the Cardiff and Bristol cases). During a discussion of the AIDS leaflet, Dr Lane *"presented the fractionator's view that a variable approach* [to the distribution of the leaflets by RTCs] *did not provide material of uniform specification"*. Surrogate tests were discussed, including the TPHA test and the anti-HBc test, but no firm conclusions were reached and logistical problems were mentioned.[266] Dr Barbara presented Dr Gunson's summary of his attendance at the Council of Europe AIDS meeting, which recommended aiming for self-sufficiency, avoiding large plasma pools (which would pose problems in the UK due to disproportionate loss of product), and providing information on AIDS to all donors. In his Proof, Dr Lane stated that the regional blood transfusion services considered surrogate testing to be inconclusive and anticipated that a marker test specific to the virus would be developed "*in due course"*.[267]

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[264] CBLA0000005_002, p.g.285-86 [650]
[265] CBLA0001729; CBLA0000005_002, pg.286, [651]
[266] Minutes of the 4th Meeting of the UK Working Party on Transfusion Associated Hepatitis, 27 September 1983, PRSE0001299, pg. 4
[267] CBLA0000005_002, p.g.288 [659]

150. Dr Lane noted, "*there may have been scope for limiting or avoiding the use of concentrates. For example, a mild haemophiliac might be treated with cryoprecipitate or simply have the operation he was due to undergo postponed whilst the AIDS risk existed. It was probable that by this stage severe haemophiliacs who had over recent years been treated with large quantities of factor VIII, much of it from commercial sources, were already infected with HIV.*"[268]

151. Referring to a meeting of the MRC Working Party on AIDS which met on 10 October 1983, Dr Lane recollected that there were no representatives of Transfusion Centres or BPL sitting on this working party, which was a DHSS initiative, set up to review scientific knowledge and research on AIDS in the UK and abroad and to encourage co-operation between researchers.[269]

152. The first meeting of the CBLA Committee for Research and Development in Blood Transfusion 's ad hoc Working Group on AIDS took place on 14 October 1983 and was attended by Dr Lane.[270] The minutes noted a general agreement that if surrogate tests were to be investigated, anti-HBc screening was preferable to TPHA.[271] The possibility of a pilot study was discussed, along with the apparent issue of regional variations of anti-HBc positives, and the issue of follow-up of donors. The Chairman stressed that the *"economical considerations"* of another test could not be ignored.

153. At the same meeting, Dr Lane outlined an investigation with respect of infectivity to NANBH with the use of smaller donor pools containing donations obtained by apheresis.[272] Preliminary results in relation to NANBH infectivity were encouraging, and if the results could be extrapolated to AIDS, the concept of small donor-pool material "*might have*

[268] CBLA0000005_002, p.g.289 [661]
[269] CBLA0000005_002, p.g.289-90 [662]
[270] Minutes of the 1st Meeting of the Working Group on AIDS in relation to Blood Transfusion, 14 October 1983, CBLA0001755
[271] CBLA0001755, pg. 2
[272] CBLA0001755, pg. 3

considerable advantages". However, the implications for plasma supply would require reconsideration.

154. At the second meeting of the CBLA's Central Committee for Research and Development in Blood Transfusion on 7 November 1983, Dr Lane provided an update on BPL's work on heat treatment and the Committee recommended to the CBLA that the BPL heat-treated Factor VIII should be subjected to clinical trials as soon as possible.[273]

155. Looking back on 1983 in his Proof, Dr Lane observed that BPL continued with its viral inactivation programme, concentrating on heat treatment, but that apart from leaflet distribution encouraging self exclusion of donors from high risk categories, the approach adopted by most was *"wait and see"* until such time as further information became available.[274]

1984

156. Dr Lane attended the second meeting of the CBLA Working Group on AIDS on 27 January 1984.[275] Dr McClelland circulated a paper outlining proposals for further action that could be taken in relation to donors found to be anti-HBc positive and there was a discussion of surrogate testing. It was agreed that a protocol for a prospective study including the probable cost involved would be drawn up prior to the next meeting of the Central Committee for Research and Development in Blood Transfusion.[276] Dr Lane reported that four or five small donor pools might be available from BPL by the end of the year.

157. The proposed study of anti-HBc surrogate tests was discussed at the meeting of the Central Committee for Research and Development in Blood Transfusion on 28 February

[273] CBLA0001766; CBLA0000005_002, pg.293, [670].
[274] CBLA0000005_002, p.g.294 [673]
[275] Minutes of the 2nd Meeting of the Working Group on AIDS in Relation to Blood Transfusion, 27 January 1984, CBLA0001799
[276] CBLA0001799, pg. 2

1984.[277] The plan was to screen 50,000 blood donor samples at the North London and Bristol RTCs, which they anticipated would produce 500 positive results. Positive donations would be separated and samples would then be subject to further laboratory investigations. It was decided that a grant application would be made to the MRC.

158. In his Proof, Dr Lane described the idea of surrogate testing as the "*personal initiative*" of Dr McClelland (Edinburgh BTC) and Dr Wallington (Bristol RTC).[278] He explained that later in the year, HTLV antibody tests were under preliminary evaluation and later the same year they appeared, rendering surrogate testing obsolete.[279]

159. Dr Lane also noted that surrogate testing was only ever "*operationally viable*" on donors at the time of donation, because the presence of HBc antibody in pools was not a reason to withdraw a pool whereas an HBc antibody in a donor might result in further investigation.[280] It would ensure rapid identification of an infected donor and also ensured that the benefits of testing blood were shared by the recipients of both cellular and plasma-based products.[281] "*A separate programme of testing plasma has always raised the question of creating dual standards of safety for recipients of cellular versus plasma products.*"

160. In April 1984, Dr Gunson prepared a note of a meeting with the Communicable Disease Surveillance Centre (CDSC), which laid out a proposed system for reporting AIDS diagnoses.[282] CDSC would inform the appropriate RTD when a patient was found to be infected with HIV or diagnosed with AIDS. Any blood donations would be traced for the previous five years, and if plasma had been sent to BPL for fractionation, Dr Lane was to be informed as soon as possible.

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[277] Minutes of the 3rd Meeting of the Central Committee for Research and Development in Blood Transfusion, 28 February 1984, PRSE0001972, pg. 3
[278] CBLA0000005_002, p.g.327 [739]
[279] CBLA0000005_002, p.g.298 [682]
[280] CBLA0000005_002, p.g.316-17 [722]
[281] CBLA0000005_002, p.g.317 [723]
[282] Note of a meeting between Dr Galbraith (CDSC), Dr McEvoy (CDSC), and Dr Gunson, "Surveillance of AIDS in relation to Blood Transfusion", 4 April 1984, CBLA0001833

161. On 19 April 1984, Dr Gunson sent Dr Lane some news briefs reproduced from the American Association of Blood Banks.[283] In his Proof, Dr Lane noted as an interesting comment the opinion of Aaron Kellner of the New York Blood Center that *"We are not convinced that AIDS is transmitted by blood transfusion... the evidence is still very shaky."* [284] The brief also reported that there was a 30% decrease in factor VIII usage and a 30% increase in cryoprecipitate use.[285]

162. Dr Lane reported in his Proof that in the autumn of 1984, HIV having been shown to be a heat labile retrovirus, final confirmation came from the US that HIV was heatl labile, which promoted the existing approach of developing a heat-treated factor VIII concentrate. [286]

163. In October 1984, an update on AIDS was published in the American Morbidity and Mortality Weekly Review which showed a marked increase in the number of AIDS cases in haemophilia patients.[287] In his Proof, Dr Lane noted the particular importance of revised advice reported from the Medical and Scientific Advisory Council of the National Haemophilia Foundation that:

a. cryoprecipitate be used in factor VIII deficient newborns and children under four and in newly identified patients never treated with factor VIII;

b. FFP be used in factor IX-deficient patients in the same categories;

c. DDAVP be used whenever possible in patients with mild or moderate haemophilia A;

[283] Letter from Dr Gunson to Dr Lane, 19 April 1984, CBLA0001838
[284] CBLA0000005_002, pg.305, [697]
[285] CBLA0001838, pg. 3
[286] CBLA0000005_002, p.g.309 [708]
[287] CBLA0000005_002, p.g.309-11 [709], referring to Morbidity and Mortality Weekly Report "Update: Acquired Immunodeficiency Syndrome (AIDS) in Persons with Haemophilia, 26 October 1984, BART0002308

d. In patients that did not fit these categories, treaters should strongly consider changing to heat-treated products with the understanding that protection against AIDS was yet to be proven, and elective surgical procedures be evaluated.[288]

164. At the meeting of the Central Committee for Research and Development in Blood Transfusion on 9 November 1984, Dr McClelland informed the meeting that a batch of factor VIII fractionated in Scotland in November 1983 had subsequently been found to contain HTLV III in August 1984[289], and the virus attack rate could be as high as 80%.[290] In his Proof, Dr Lane observed that the "*salutary effect of this dreadful problem which Scotland experienced with just one batch of factor VIII was considerable.*"[291]

[288] CBLA0000005_002, p.g.309-11 [709], referring to BART0002308, pg. 3
[289] This date may be a mistake.
[290] Minutes of the 4th Meeting of the Central Committee for Research and Development in Blood Transfusion, 9 November 1984, CBLA0001919
[291] CBLA0000005_002, p.g.313 [713]

Screening of Donors and Testing for HIV

Introduction

165. Dr Lane asserted that the first commercially available US tests were licensed around March 1985, but were considered unsatisfactory in the UK because of their false positivity rate.[292] The UK, by contrast, was, he said, developing a test based on a method known to minimise false positive reactions which was available for routine use by October 1985.

166. By the time commercial tests were available in February 1985, BPL/PFL had stopped releasing non-heat treated factor VIII concentrate. Subsequent follow-up of heat-treated product confirmed full viral inactivation of HIV in the limited study of intermediate concentrate HL and 8CRV as well as, in due course, 8Y and 9A.[293]

167. According to Dr Lane, testing for HIV for both plasma and end product was introduced at BPL/PFL in December 1985, weeks after the introduction of testing at RTCs (the 5th draft contained a note for Dr Lane to insert the exact date, but this paragraph was missing from the 6th draft).[294] He explained that antibody testing gave information on the history of infection but the implication for infectivity was not necessarily direct because some antibodies imply recovery from infection.[295]

1983

168. At the meeting on AIDS at BPL on 18 April 1983 (referred to earlier in this presentation), it was agreed that it would be difficult for BPL to respond to a request to make small pool material or heat-treated product.[296]

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[292] CBLA0000005_002, p.g.316 [719]
[293] CBLA0000005_002, p.g.316 [721]
[294] CBLA0000005_002, p.g.317 [724]
[295] CBLA0000005_002, p.g.317 [725]
[296] Notes of a Meeting held on 18 April 1983, BPLL0008758

169. Subsequently, research was carried out through the Oxford small pool experiments, which Dr Lane described as unsuccessful for NANBH and how successful it would have been for HIV, a matter for speculation.[297] He opined that, "*it would have been a tremendous upheaval not just for BPL/PFL but also for Regional Transfusion Centres to take an about turn and attempt to establish a small pool system at a time when simply not enough was known about the causative agent of AIDS to form any considered view as to whether such an approach would, in any event, be successful.*" Instead, they concentrated their efforts on heat treatment, taking their lead from published scientific literature so far as it existed.

1984

170. On 21 May 1984, Dr Tyrrell, the Chairman of the MRC Working Party on AIDS, wrote to Dr Gunson, referencing the papers by Montaigner and Gallo and suggesting that these advances would mean it would be possible to look for antibodies using a routine ELISA test.[298] He offered the assistance of the MRC Committee in acquiring the technology and setting up a study. Dr Lane observed in his Proof that this letter was written against the background of the confirmed identification of the virus which was thought to be the cause of AIDS.[299]

171. In August 1984, Dr Harris wrote to Dr Lane, inviting him to join the Advisory Committee on the NBTS Working Group on AIDS.[300] He wrote that with the recent development of a radioimmunoassay technique for the detection of antibody HTLV III, it was necessary for a group of experts to consider the implications for the NBTS.

172. At the Advisory Group on Hepatitis meeting on 9 October 1984, at which Dr Lane was present, Dr Craske presented an update on AIDS and informed the meeting that a reliable immunoassay procedure had been developed at the Middlesex Hospital Medical

[297] CBLA0000005_002, p.g.322 [732]
[298] Letter from Dr Tyrrell to Dr Gunson, 21 May 1985, CBLA0001847
[299] CBLA0000005_002, pg.334, [749]
[300] Letter from Dr Harris to Dr Lane, 31 August 1984, CBLA0001875

School.[301] Dr Lane's Proof stated that this was the earliest major RIA development test in the UK.[302]

173. On 12 October 1984, Dr Lane wrote to Dr Harris at the DHSS, informing him that BPL was planning dried heat treatment of all factor VIII and urging that the UK adopt a strict approach to specification of imported labile blood products, similar to the recent strict requirements introduced by the German government.[303] He added that the recent discussion at the Advisory Group on Hepatitis led him to believe his views were "*widely supported*". In his Proof, Dr Lane explained that he was advocating a review of specification for products imported into England and Wales, but was not advocating a ban of those products.[304]

174. Dr Harris replied to Dr Lane on 8 November 1984, writing:

> *"As far as your proposal to heat treat factor VIII is concerned, I would hope that you would bring this to the attention of the Advisory Group who might wish to consider if the evidence for inactivation of HTLV III by heat is sufficient to warrant taking this step, particularly if a screening test can be made available. There may also be implications for the adequacy of the proposed plasma supply if heat treatment affects the yield of factor VIII harvested which both the CBLA and the Department would need to have clarified. I trust that you will furnish both the Department and the CBLA with full details of this proposal."*[305]

175. In his Proof, Dr Lane described this letter as "*very unusual*", given that they were so advanced with the heat treatment work, which Dr Harris was well aware of.[306]

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[301] Minutes of the meeting of the Advisory Group on Hepatitis, 9 October 1984, CBLA0001904, pg. 5
[302] CBLA0000005_002, pg. 337, [757]
[303] Letter from Dr Lane to Dr Harris, 12 October 1984, CBLA0001907
[304] CBLA0000005_002, p.g.339 [759]
[305] Letter from Dr Harris to Dr Lane, 8 November 1984, CBLA0001916
[306] CBLA0000005_002, p.g.340-41 [763]

176. On the same day, 8 November 1984, a meeting of the Advisory Committee on the NBTS took place, chaired by Dr Harris and attended by Dr Lane. Dr Smithies (DHSS) advised the meeting that the Middlesex Hospital and Chester Beatty Laboratory were testing for HTLV III antibody using an RIA method. Dr Lane asked for an update on both the Gallo and British isolate availability, to which Dr Smithies responded that the US had been approached for permission to use the Gallo isolate in the UK and some progress had been made on the British isolate.[307] A further update was provided at the meeting of the CBLA Central Committee for Research and Development in Blood Transfusion on 9 November 1984.[308]

177. The first meeting of the Working Group on AIDS was held on 27 November 1984.[309] In his Proof, Dr Lane described the meeting as *"unproductive"* and explained he had a disagreement with the Chairman, Dr Abrams, as Dr Lane had thought that the introduction of the HTLV III test should be accelerated.[310] Dr Abrams had commented that if BPL was short of money to make an HIV antibody test, it was due to the overspending on the BPL redevelopment. Dr Lane had taken great exception to this comment and had written to Mr Smart on 28 November 1984 to record his objection.[311] Dr Lane explained that the meeting was not particularly effective because *"the question of what tests were to be developed and introduced and how they were to be applied was largely a financial one, for which the DOH was responsible for clear guidance on policy, subject to advice from experts."*[312]

178. Dr Lane called the meeting of the Haemophilia Reference Centre Directors, Blood Transfusion Service advisors and BPL plasma fractionation staff on 10 December 1984.[313] The meeting discussed the problems regarding the introduction of HTLV III antibody screening, including the difficulty in obtaining isolates, the cost of the kit, the extra staff required and what advice should be given to donors found to be HTLV III positive.

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[307] PRSE0004783
[308] CBLA0000005_002, pg.341, [764]; CBLA0001919.
[309] Minutes of the 1st Meeting of the Working Group on AIDS, 27 November 1984, CBLA0011985
[310] CBLA0000005_002, p.g.352-53 [776]
[311] Letter from Dr Lane to Mr Smart, 28 November 1984, CBLA0001937
[312] CBLA0000005_002, p.g.352-53 [776]
[313] Minutes of a meeting of Haemophilia Centre Directors and BPL, 10 December 1984, CBLA0001948

Limited resources made it impossible to do routine tests on haemophilia patients. Dr Lane suggested BPL could play a part in coordinating testing if resources were available.

179. The meaning of an HTLV III antibody positive result was also discussed at the meeting.[314] It was noticed that some patients did not produce antibodies, so an infected batch would not always result in the detection of antibodies in patients who had received the batch. Dr Ludlum confirmed that in Scotland some patients who were previously antibody positive were now negative.

180. Commenting upon this meeting in his Proof, Dr Lane noted that the DHSS was "*effectively being held responsible for determining the future course of testing. On behalf of BPL, I offered to assist with development and distribution of an HIV antibody test along the lines of a test established earlier for HBsAG.*"[315]

1985

181. At the CBLA meeting on 1 February 1985, Dr Lane advised that, if given the antibody, BPL could produce an alternative test at a much lower cost.[316] The minutes also recorded that it was considered vital that a British test be developed. In his Proof, Dr Lane explained that the introduction of an ELISA test for HIV antibody would require alternative equipment in all centres, whereas the BTS was already equipped for radioimmunoassay testing.[317] He also noted that nothing came of the offer for BPL to be involved in developing an RIA test.[318]

182. The first commercial tests for HTLV III were licensed by the FDA in March 1985. [319] Dr Lane claimed that these tests had an unacceptably high level of false positives, which implicated advice to donors and created problems with secondary testing.

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[314] CBLA0001948, pg. 3-4
[315] CBLA0000005_002, p.g.349 [769]
[316] Minutes of the 16th Meeting of the CBLA, 1 February 1985, DHSC0002325_040, pg. 6
[317] CBLA0000005_002, p.g.354 [780]
[318] CBLA0000005_002, p.g.354 [781]
[319] CBLA0000005_002, p.g.355 [784]

183. Dr Lane wrote in his Proof that BPL's position on the introduction of testing was:

> *"...not to pre-empt the introduction of testing in the Regional Transfusion Centres insofar as it has always been a policy to adopt the standard of testing used by the BTS for the blood to be transfused and plasma to be used for fractionation. We were following the progress of testing which might be appropriate for validation on the finished products (but as I have already said, these are not representative of whole plasma). Our security of product was believed to come through the introduction of heat inactivation insofar as the antibody screen would not necessarily guarantee the non-infectivity of all plasma."*[320]

184. He continued:

> *"The validity of the tests becoming available created some real cause for doubt and there was the question of sensitivity: we did not believe the incidence of HIV in the donor community at that time was high and this was subsequently shown to be true. Therefore, there was a lot of uncertainty about the relevance of the test at that time."* [321]

185. The question of testing came up at the meetings of the Central Committee for Research and Development in Blood Transfusion, held on 2 April 1985[322] and on 9 July 1985.[323] At the latter meeting Dr Gunson expressed his view that, until a proper evaluation of the tests had been carried out within PHLS and the BTS, the tests should not be used for the routine screening of blood donations.[324] Professor Bloom disagreed, and said that whilst he appreciated the need for a proper evaluation, his immediate priority was the protection of recipients and considered any undue delay in their introduction

[320] CBLA0000005_002, p.g.358-59 [790]
[321] CBLA0000005_002, p.g.359 [791]
[322] CBLA0002113; CBLA0000005_002, pg.356. [787]
[323] Minutes of the 6th Meeting of the Central Committee for Research and Development in Blood Transfusion, 9 July 1985, BPLL0004117
[324] BPLL0004117, pg. 3

unreasonable. Dr Lane informed the meeting that excess plasma products released onto the market from BPL were likely to require licensing by the FDA, which would make the routine screening of donations by an FDA-approved test a requirement.

186. In Dr Lane's Proof, he wrote that by September 1985, Organon and Wellcome tests were nearing approval.[325] The assessment of all tests was carried out by the PHLS who reported to the DHSS. BPL was waiting for the BTS to introduce donor testing, and the choice of test was made on advice given by the PHLS and the DHSS, as did the timing of its introduction.

187. On 27 September 1985, the "*Interim Report on Survey of HTLV Antibody in Haemophiliacs in the UK*" was prepared at the Oxford Haemophilia Centre, based on returns from 79 Haemophilia Centres.[326] 2,420 patients were tested, with 44% of haemophilia A patients found to be positive, and 6% of haemophilia B patients. In his Proof, Dr Lane stated that, "*although factor IX was less likely to transmit HIV based on the manufacturing process used, I cannot help speculating, as indeed I have done previously, that this might in part be evidence supportive of the contention that blood products made from English and Welsh plasma donations would have been inherently safer than the equivalent commercial product so far as HIV was concerned.*"[327]

188. According to Dr Lane, full anti-HTLV III screening was introduced at RTCs on 14 October 1985 and testing of finished product at BPL was introduced in December 1985.[328]

Summary of AIDS/AIDS Risk Claims and Screening of Donors and Testing for HIV

189. In response to an allegation that the CBLA should have been aware of the emergence of AIDS and its implications and acted in light of that, Dr Lane stated that:[329]

[325] CBLA0000005_002, p.g.367 [800]
[326] Interim Report on Survey of HTLV Antibody in Haemophiliacs in the UK, 27 September 1985, HCDO0000518
[327] CBLA0000005_002, p.g.367 [801]
[328] CBLA0000005_002, p.g.368 [804-5]
[329] CBLA0000005_002, p.g.373-74 [812]

"...all interested parties including CBLA were as up to date as possible at any particular time given that the majority of information was, at least initially, generated in the United States and only subsequently was research undertaken in the UK. The CBLA pressed forward with its research into inactivation of viruses using heat treatment and development of processes to be applied to factor VIII and factor IX concentrates in the light of scientific information, confident that it would be a solution to the HIV problem, as events subsequently showed... the alternative of small pool methods of manufacture would not have been practicable and in any event would not have offered total protection against HIV, given that we were only in a position to provide a proportion of the factor VIII required for the treatment of haemophiliacs in England and Wales. We were committed to the research we were carrying out on heat treatment and by the time HIV was identified and found to be heat labile, we were poised to introduce a new high purity concentrate which was extremely tolerant to heat treatment and in the interim, we acted by making available the existing intermediate product in a heat treated form in replacement of non-heat treated factor VIII."

"...The priority for any fractionator is an inactivation process for viruses. Progress with the control of Non-A Non-B hepatitis is a precise example of this, where the fractionator controlled transmission of this virus before it had been defined, or visualised or a marker test produced. At the end of the day, screening does not avoid virus activity in the fractionation process."[330]

190. In response to an allegation that the CBLA should have been keeping itself informed of advances in learning and experience in respect of AIDS, Dr Lane repeated that at any given time, the CBLA was "*as up to date as anyone could be with regard to AIDS",* as evidenced (he said) by the regular meetings of experts and membership of various Working Parties.[331]

[330] CBLA0000005_002, p.g.374 [813]
[331] CBLA0000005_002, p.g.374 [814]

191. In response to an allegation that from 1982 the CBLA should have known of the growing suspicion in the USA of a connection between AIDS and the supply and use of blood products and acted in light of that, Dr Lane stated that "*it should be noted that very limited information came from the US during 1981 and, of course, this was very early in the history of AIDS with the result that there were no clear indications at all as to quite what caused AIDS.*"[332] By mid-1982 the first suggestions that AIDS might be linked with blood transfusion and blood products appeared in scientific literature, but Dr Lane argued "*whilst this link could be speculated upon, the agent at work was completely unknown, and there were only a few reported cases in the US and none in the UK.*"[333]

192. Dr Lane asserted that it was not until the spring of 1984 that the causative agent for AIDS was confirmed, by which time their heat treatment research, "*which was clearly the only practical solution to the HIV problem, aside from screening*", was well advanced.[334]

193. Dr Lane argued that even if one accepted, which he did not, that it was possible to infer that the causative agent of AIDS was a virus susceptible to heat treatment from 1981, 1982 or 1983, "*it is difficult to see how our programme of research and development into heat treated products could have been accelerated, with respect to HIV (then generally undefined when the programme was oriented to inactivation of hepatitis NANB).*"[335] In retrospect, early commercial heat-treated products were not safe in respect to NANBH and some also failed to inactivate HIV.

194. In response to an allegation that there was a failure, from 1982, to reduce the risk by requiring the reduction of pool sizes of donated blood for home-produced product or advising such reduction, Dr Lane stated that the Oxford small pool experiments were not successful in relation to NANBH and it was uncertain what, if any, protection small pools would have provided for HIV.[336] Moreover, "*such a massive re-ordering of the approach*

[332] CBLA0000005_002, p.g.374-75 [815]
[333] CBLA0000005_002, p.g.375 [816]
[334] CBLA0000005_002, p.g.375 [817]
[335] CBLA0000005_002, p.g.375-76 [818]
[336] CBLA0000005_002, p.g.378 [821]

to producing concentrates would have been a major undertaking, even had it offered the prospect of material protection." He repeated that large pools were used in England, Scotland, the US and Europe, and for severely affected haemophilia patients, frequent recourse to treatment would involve equivalent donor exposure, whether from fewer large pool products or greater numbers of small pool products.

195. In response to an allegation that there was a failure to consider the possibility of surrogate testing, Dr Lane argued that "*surrogate testing was really not possible until such time as a reasonable amount of information regarding the cause of AIDS was available. In my view not enough was known until the actual identification of HIV which occurred in the early part of 1984."*[337] The anti-HBc approach was pursued, but was quickly made redundant by the work of commercial pharmaceutical companies on a test for the HIV antibody "*which was clearly much more productive"*.

[337] CBLA0000005_002, p.g.379-80 [826]

Heat Treatment

196. Dr Lane's Proof explained that in the early 1970s, the main form of treatment for haemophiliacs, cryoprecipitate, could not be heat treated. As the use of concentrates grew, so did knowledge of the risk of HBV infection.[338] Dr Lane argued that this risk was mitigated through the use of donor screening and later by the immunisation of patients.[339]

197. He stated that by the end of the 1970s "*knowledge of the existence of NANB [non-A non-B] hepatitis had reached the point where it could be said that infection was virtually inevitable the moment a patient was treated with concentrate for the first time (whether commercial or NHS).*"[340] He argued that viral inactivation was not explored earlier because:

a. It was believed factor VIII was too unstable, owing to the significant reduction in yield which followed attempts to increase purity.[341] The loss of yield was not fully justified, as the economics of factor VIII yield meant that best use must be made of the plasma available.

b. They were aware that early attempts by commercial manufacturers to heat treat products had resulted not only in severe loss of yield, but also had failed to eradicate virus transmission.[342]

c. BPL's first action was to review all the likely virus inactivation methods available, with research beginning in the area of pasteurisation.[343]

d. "*The policy of the Transfusion Service and the DOH was aimed at the maximum provision of factor VIII concentrates for the treatment of haemophiliacs since it was considered that this represented the primary*

[338] CBLA0000005_002, p.g.385 [839]
[339] CBLA0000005_002, p.g.385 [840]
[340] CBLA0000005_002, p.g.386 [842]
[341] CBLA0000005_002, p.g.386 [843]
[342] CBLA0000005_002, p.g.387 [844]
[343] CBLA0000005_002, p.g.387 [845]

benefit to the patient, i.e. to arrest bleeding. Whilst it was understood that hepatitis B infection was a hazard of treatment, the risk benefit ratio was clearly with the control of bleeding."[344]

e. It was only from the early 1980s that it was known that NANB hepatitis was *"unacceptably common and potentially life threatening"* that *"attention had to be given"* to virus inactivation processes.[345]

1981

198. In his Proof, Dr Lane described the requirement for central funding for research and development of heat treatment as a *"continuous theme"* of 1981.[346] Methods of viral inactivation were raised by Dr Lane in February 1981, when he invited staff to set out projects[347], leading to a proposal for their development being submitted for DHSS funding. [348] The proposal related to the development of methods for the production of concentrates with reduced risk of hepatitis transmission. An (undated) paper produced by BPL's Research and Development department described various methods of inactivation, noting that heating albumin in the presence of a stabiliser had a good record in eliminating hepatitis virus, and that if similar stabilisers could be found for factor products, then heat inactivation would become the treatment of choice.[349]

199. Dr Lane discussed reducing hepatitis with Dr Smith and Dr Harvey on 14 September 1981.[350] His note of the meeting recorded that a point was made that various commercial manufacturers had now produced factor products claiming to have *"substantially reduced the risk of hepatitis"*. These claims *"may lack scientific integrity"* but created ethical pressure on clinicians to use such products.

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[344] CBLA0000005_002, p.g.387 [847]
[345] CBLA0000005_002, p.g.387 [847]
[346]CBLA0000005_002, p.g.391 [855]
[347] Memo from Dr Lane dated 13 February 1981, BPLL0005475
[348] CBLA0000005_002, p.g.389 [848], referring to "Proposal for support of a Research Project", dated 27 February 1981, CBLA0001291
[349] CBLA0001401
[350] Note of discussions held with Dr Harvey and Dr Smith, 14 September 1981, CBLA0001446

200. The BPL/PFL annual report for the year 1981/82 made no reference to research on inactivation of viruses by heat treatment in 1981, and Dr Lane acknowledged in his Proof that no time was spent on this in 1981, with work only really starting (in relation to Factor IX) in 1982.[351] Dr Lane's Proof also drew attention to an address on inactivation by Dr Smith on 24 November 1981, with the comment that *"Our thoughts were beginning to turn to this subject as the link between non-A non-B hepatitis and chronic active hepatitis increased and, with it, the desirability of inactivating the hepatitis virus if we could"*.[352]

1982

201. Dr Lane observed in his Proof that during the course of 1982 discussions directed at viral inactivation were aimed at reducing infectivity of HBV; *"It was only towards the end of the year, that there was real recognition of a possible risk of HIV infection for haemophiliacs treated with blood products"*.[353]

202. On 5 April 1982, Dr Lane circulated a memo to employees of BPL referring to a trial of Polyelectrolyte VIIIC, a process which produced very high quality factor VIII which did not appear to transmit NANB hepatitis.[354] In his Proof, Dr Lane explained that the end product was not stable and further development was not carried out because funding could not be agreed with Speywood, who had pioneered the process.[355]

203. At the Hepatitis Working Party meeting on 13 September 1982, attended by Dr Lane, there was a discussion of the "*hepatitis reduced"* Hemofil and a new method of pasteurisation in the presence of polysaccharides patented by Biotest Laboratories in Germany, which would, according to the minutes, need to be evaluated by chimpanzee

[351] Dr Lane, Annual Report 1981/2 for BPL/PFL, 20 April 1982, CBLA0001570; CBLA0000005_002, pg. 394, [864]
[352] CBLA0000005_002, pg.393, [861]
[353] CBLA0000005_002, pg.395, [865].
[354] Memo from Dr Lane to Dr Harvey, Mr Mallory, Dr Smith, Mr Snape and Mr Vallet, 5 April 1982, CBLA0001566
[355] CBLA0000005_002, pg. 395, [867]

inoculation or a prospective study in susceptible human subjects.[356] In his Proof, Dr Lane recalled that there was in fact a German product Humate produced by Behringwerke in about 1980 using a wet heat pasteurisation process.[357] He stated that this product was never licensed and factor VIII yield was only 7% to 10%.

204. On 13 October 1982 Dr Lane sent a memo to Dr Harvey explaining that he would shortly be calling for a meeting to set out plans for studies on pasteurisation. He was interested to know what information was available about detergents in a role which might be supportive to Factor VIII during the exposure to heat.[358]

205. On 15 December 1982, an informal meeting took place at BPL (at Dr Lane's request, according to his Proof) to discuss the implications of the commercial *"hepatitis-safe"* factor VIII and IX.[359] Dr Lane's purpose in calling the meeting was to ascertain what a representative sample of HCDs wanted, as he did not want to direct a course of research and development into a product which thereafter failed to gain acceptance. [360]Concerns were raised that these products were being used without having been licensed and therefore were not subject to a properly controlled trial. Dr Lane's note of the meeting proposed that the *"random exploitation"* of haemophilia services by commercial organisations to study their *"hepatitis-safe"* products be discouraged, and controlled clinical trials should be created.

206. Following the meeting, Dr Lane produced a file note which recorded that none of the *"hepatitis-safe"* commercial products were guaranteed free of transmission risk of hepatitis; the methods involved tended to carry substantial penalties in yield; treatment methods were not sufficiently close to existing production methods that they constituted appropriate examples for variation orders to existing licences; and evidence of satisfactory inactivation could only be demonstrated in chimpanzees for routine quality control

[356] Minutes of the 10th Meeting of the UK Haemophilia Centre Directors Hepatitis Working Party, 13 September 1982, HCDO0000556
[357] CBLA0000005_002, p.g.396-7 [871]
[358] CBLA0001633.
[359] Minutes of a meeting at BPL, 15 December 1982, CBLA0001649
[360] CBLA0000005_002, pg.398, [876]

purposes.[361] Dr Lane's view was that *"the commercial products should have been subject to a clinical trial and then licensed"*. To be licensed, the manufacturer would have to show the product had a standardised process, how the process worked, and that the process could be reproduced.[362] He noted that none of the commercial manufacturers were describing their heat treatment or stabilisers with accuracy.[363] He believed that studies were important because of the likelihood that heat treatment could introduce structural changes to proteins which could induce antibody development against factor VIII.[364]

207. An exchange of letters between Dr Cash and Dr Lane in December 1982 referred (in Dr Cash's words) to *"furtive arrangements"* between Dr Smith and Dr Foster as regards Factor VIII; Dr Lane commented in his Proof that the arrangements in question were not furtive but *"quite open and were intended to share knowledge and information about heat treatment experimentation"*.[365]

1983

208. In February 1983, Dr Lane prepared a memo setting out progress with the establishment of a committee to deal with internal R & D at BPL. The list of research projects with the highest priority included inactivation of transmissible virus in protein fractions.[366] The same month Dr Smith prepared a paper *"Proposal to develop a "hepatitis-safe" factor VIII concentrate"*.[367] It noted that factor VIII had always been regarded as *"exceptionally labile"*, and only recently had serious attempts been made to apply physical and chemical processes to inactivate hepatitis viruses. The options were immunological neutralisation, physical removal of infective agents or inactivation by heat or virucides. Dr Smith concluded that heating was the most promising approach because it was likely to be of broad application; the treatment was cheap, relatively easily controlled,

[361]CBLA0000005_002, p.g.402 [885], CBLA0001661.
[362]CBLA0000005_002, p.g.403 [887]
[363]CBLA0000005_002, p.g.403 [888]
[364]CBLA0000005_002, p.g.405 [892]
[365] CBLA0000005_002, pg. 400, [881]; CBLA0001650; CBLA0001651
[366] CBLA0001681
[367] "Proposal to develop a "Hepatitis-Safe" factor VIII Concentrate", February 1983, CBLA0001781

recorded and scaled up with precision; and extensive experience with other successful pasteurised proteins such as albumin offered readier regulatory and clinical acceptance.[368]

209. At the meeting of key BPL staff on 18 April 1983, it was agreed that BPL should proceed with heat-treated products, despite fears over yield.[369] Deadlines for draft proposals were set for 15 July 1983, which Dr Lane claimed demonstrated their *"commitment at that point to progress as far and as fast as possible the development of heat treated factor VIII."* [370]

210. Dr Smith's memorandum to Mrs Winkelman dated 23 June 1983 stated that the heat treatment project was given A1 priority, i.e. most important to BPL/PFL's immediate product strategy; Dr Lane's Proof stated that he confirmed the priority level of this work.[371]

211. Dr Craske's paper for the Hepatitis Working Party dated 11 July 1983 outlined the various products available as:

a. freeze dried product heated in the presence of compounds (e.g. sucrose) which stabilised the factor VIII activity, such as Hemofil T;

b. products made from plasma treated with chemicals, such as Kryobulin; and

c. product pasteurised by heating at 60 degrees celsius in the presence of stabilisers for factor VIII, such as Behringwerke's product.[372]

212. The paper noted that: *"a choice will have to be made between using heat treated products from commercial sources, which might carry a small risk of AIDS transmission, or*

[368] CBLA0001781, pg. 4
[369] Notes of a Meeting held on 18 April 1983, BPLL0008758
[370] CBLA0000005_002, p.g.410-11 [910]
[371] Memo from Dr Smith to Mrs Winkelman, 23 June 1983, CBLA0001718; CBLA0000005_002, pg.412 [915]
[372] J. Craske, "Factors to be considered in the Selection of Hepatitis Reduced Products for Clinical Trial", 11 July 1983, HCDO0000135_012, pg. 1

using NHS concentrate which appears to carry a 100% chance of transmitting non-A, non-B hepatitis".[373]

213. Dr Lane's memo on AIDS dated 26 July 1983 reported that wet heat appeared a less satisfactory route for research than dry heat, and the majority of commercial manufacturers were using dry-heat.[374] BPL had undertaken preliminary studies to assess yield of factor VIII intermediate concentrate after dry-heat and the product was being "*advanced with high priority to enable manufacture to become routine by the late summer 1984".*

214. In the minutes of the first meeting of the CBLA Working Group on AIDS, held on 14 October 1983, attended by Dr Lane, it was noted that dry-heat treatment of factor VIII and factor IX had not initially been encouraging from the studies on chimpanzees.[375]

215. In his Proof, Dr Lane wrote that "*AIDS very quickly eclipsed the idea of carrying out detailed studies on products which might potentially offer protection."*[376] For instance, he said, at the 12th Meeting of the UK Haemophilia Centre Directors' Hepatitis Working Party, concern was expressed that it was unknown whether inactivation procedures used in various products inactivated the AIDS virus, and *"any Director considering using the commercial products in such a clinical trial would, therefore, have to take this into account."*[377]

216. In November 1983, at the 2nd Meeting of the Central Committee for Research and Development in Blood Transfusion, Dr Lane reported that a dry heat-treated BPL product was available for trial.[378] The Committee recommended that the product be subjected to clinical trials as soon as possible, given the possibility that commercial companies might

[373] HCDO0000135_012, pg. 3
[374] Dr Lane, "AIDS, progress with heat treatment of human plasma products", 26 July 1983, CBLA0001729
[375] Minutes of the 1st Meeting of the Working Group on AIDS in relation to Blood Transfusion, 14 October 1983, CBLA0001755
[376] CBLA0000005_002, p.g.419 [930]
[377] DHSC0001670 and CBLA0001536
[378] Minutes of the 2nd Meeting of the Central Committee for Research and Development in Blood Transfusion, 7 November 1983, CBLA0001766, pg. 3

shortly introduce such a product *"with its attendant publicity"* which might present Haemophilia Directors with a dilemma.

217. In his Proof, Dr Lane described the Haemophilia Centre Directors he approached as showing *"no immediate enthusiasm"* to use the new BPL product on a trial basis, and they only secured three patients who received heated 8CRV in 1984.[379] Their efforts to obtain a proper trial were unsuccessful, but meanwhile the problem of AIDS had developed to the point that by end of 1984 it was clear they would have to introduce the heat-treated product even though it had not been validated clinically in more than these 3 patients.[380]

218. Dr Lane observed further in his Proof that they continued research *"against the background of considerable uncertainty as to the effectiveness of the final product: HIV changed priorities and an orderly approach towards clinical evaluation of virus inactivation which might have proved possible in the context of hepatitis NANB was overtaken by events."*[381] By 1983 and 1984, HIV had given *"considerable impetus"* to research and development work.[382]

219. In Scotland, PFC introduced heat treatment of factor VIII earlier than BPL, but only applied what Dr Lane described as *"marginal amounts of heat"*. Dr Lane wrote that he saw no point in applying this method which was unlikely to be wholly effective for NANB hepatitis or HIV.[383]

1984

220. On 3 January 1984, Dr Smith produced a memo entitled *"Proposal for special preparation - 8CRV pasteurised dry"*.[384] It summarised the motivations behind the decision

[379] CBLA0000005_002, p.g.420 [932]
[380] CBLA0000005_002, p.g.420 [933]
[381] CBLA0000005_002, p.g.407 [899]
[382] CBLA0000005_002, p.g.387 [846]
[383] CBLA0000005_002, p.g.408 [901]
[384] Memo from Dr Smith to Dr Lane, 3 January 1984, CBLA0001786

to dry heat 8CRV, including the need to offer *"at least some hope"* of reduced risk of transmitting AIDS, the suggestion in Hyland's study that infectivity of NANBH had been reduced, and BPL/PFL's *"late start"* in more rigorous inactivation studies which might leave BPL/PFL without product for a year or more, by which time *"many of the small group of suitable patients would have been committed to testing other products.*[385] In his Proof, Dr Lane asserted that this reference to a *"late start"* should not be misunderstood and indicated their intention *"to define a heat treatment process capable of full virus inactivation, probably requiring more severe heating than was currently recognised."*[386]

221. In Dr Lane's report dated 16 January 1984, he summarised the research and development on product safety and yield between April 1982 and December 1983.[387] Conditions had been established for dry heating concentrates, and a trial of these products was expected to precede that of concentrated heated in solution.[388] He reported that it seemed likely that factor IX could be pasteurised with less than 50% reduction in overall yield.

222. In his Proof, Dr Lane stated that, whilst efforts were still directed at a "*hepatitis-safer*" form of concentrate, experience suggested that NANB hepatitis was a tough virus, so that if it could be inactivated, it was expected that the treatment would affect a number of other less robust viruses.[389]

223. Dr Lane received an update from Dr Smith in July 1984 on cases where individual patients had been treated with NHS heated Factor VIII, with Dr Smith observing that it was *"an encouraging start".*[390]

224. On 12 October 1984, a memo from Dr Snape to Dr Smith and Mr Wesley recorded that Dr Lane had asked that urgent consideration be given to the possibility of introducing a

[385] CBLA0000005_002, p.g.422-3 [938]
[386] CBLA0000005_002, p.g.423 [939]
[387] Dr Lane, BPL Report April 1982 - April 1983, April 1983 - December 1983, 16 January 1984, DHSC0002239_003
[388] DHSC0002239_003, pg. 40
[389] CBLA0000005_002, p.g.425 [943]
[390] Memo from Dr Smith to Dr Lane dated 11 July 1984, CBLA0001865; CBLA0000005_002, pg. 428, [954]

dry-heating step to factor VII and factor IX concentrates as routine, aimed principally at the elimination of AIDS, and *"accepting the dubious effectiveness of dry heating and the prevention of NANB hepatitis transmission."*[391] Dr Lane observed in his Proof, by reference to a summary received in October from Dr Smith concerning work on the 8Y project, that *"It was clear that 8CRV and HL were unsatisfactory for vigorous heat treatment, and the 8Y project was aimed at producing a product which overcame the problems and, in essence, had a greater purity"*.[392]

225. Dr Lane wrote to Dr Harris at the DHSS on 12 October 1984, informing him that BPL was actively planning dried heat treatment of all factor VIII.[393] Dr Harris' response was, in Dr Lane's view, *"not favourable"*.[394] Looking back, he wrote that:

> *"Nonetheless, we were by now pressing ahead with heat treatment in any event. It seemed to me that whilst there were penalties involved, the risks of transmission of HIV were such that heat treatment should be employed even if it turned out to be a temporary expedient. There was no generally applicable test for HIV at the time, but we knew from our research work on heat treatment, that heat treatment was feasible and, in the longer term, the development of a superior product (8Y) carrying less penalty in terms of loss of yield due to heating and greater possibilities of virus inactivation because of its tolerance to heat, was beginning to look a firm possibility."*[395]

226. At the meeting of the Central Committee for Research and Development on 9 November 1984, Dr Lane reported that BPL was dry heating factor VIII with no great loss of yield, and estimated the timescale for the new product as approximately one year.[396] It was agreed to recommend to the CBLA that BPL should commence dry heat-treating

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[391] Memo from T. J. Snape to Dr Smith and Mr Wesley, 12 October 1984, CBLA0001908
[392] CBLA0000005_002, pg. 431, [962]
[393] CBLA0001907
[394] CBLA0000005_002, p.g.431 [963]
[395] CBLA0000005_002, p.g.432 [965]
[396] Minutes of the 4th Meeting of the Central Committee for Research and Development in Blood Transfusion, 9 November 1984, CBLA0001919, pg. 2

material currently being produced, whilst examining methods to obtain a better yield so that wet heat treatment might be feasible.

227. A memo on heat treated concentrates was sent to Dr Harvey on 12 November 1984.[397] It reported that of the three patients who had received large doses of dry heated 8CRV in 1984, none had contracted hepatitis or AIDS. Incomplete clinical trials of commercial factor VIII suggested that NANBH transmission was only reduced by 30%.[398] Considering the lack of good clinical data, and with the suspicion that virus kill might vary between batches, it noted that dry-heating had not been considered more than a stop-gap at PFL but that very recent data made dry-heating attractive as an immediately practical and minimally invasive way of reducing the transmission of AIDS, if not NANBH.

228. At a BPL meeting on 13 November 1984, it was recorded that little definite information existed about the efficacy of heat treatment, nor on the loss of specific activity.[399] It was agreed that, for the time being, heating for 24 hours at 70°C represented a reasonable compromise. It was recognised that every effort must be made to start heat treatment as soon as possible, and Dr Lane would be consulted in an attempt to by-pass some of the formal tendering requirements.[400]

229. At the CBLA Meeting on 28 November 1984, the minutes recorded that the authority approved the expenditure of £72,000 for ovens for trials of heat-treated factor VIII from the intermediate capital cash limit.[401]

230. At the meeting of Haemophilia Reference Centre Directors held at BPL on 10 December 1984, Dr Lane explained that heat treating BPL product had led to a 15-20% loss of output.[402]

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[397] Memo from Dr Smith, Dr Evans, Mrs Winkelman and M. E. Haddon to Dr Harvey, 12 November 1984, CBLA0001920
[398] CBLA0001920, pg. 2
[399] Memo from Mr Wesley containing summary of meeting on 13 November 1984, 19 November 1984, CBLA0001923
[400] CBLA0001923, pg. 2
[401] Minutes of the 15th Meeting of the CBLA, 28 November 1984, ç, pg. 4
[402] Minutes of a meeting of Haemophilia Centre Directors and BPL, 10 December 1984, CBLA0001948

231. Following the meeting, an AIDS Advisory Document was prepared for Haemophilia Centre Directors dated 14 December 1984.[403] The document recommended that patients not previously exposed to concentrate and children be treated with cryoprecipitate or heat-treated NHS factor VIII if available.[404] Severe and moderate haemophilia patients previously treated with factor VIII were recommended to use heat-treated NHS factor VIII if available or heat-treated US commercial factor VIII. Haemophilia B patients were advised to use FFP or NHS factor IX concentrate if essential. Mild Christmas Disease patients were recommended to use FFP if possible, otherwise NHS factor IX.

232. The document noted that BPL could not take back unused, unheated concentrate for reissue.[405] In his Proof, Dr Lane explained that this was because of quality control; they did not know how the products had been handled during transportation and storage.[406] They also did not have the capacity to heat treat recalled product: they would have received only "part" batches, so ovens would have been part filled, substantially reducing efficiency.

233. Mr Pettet wrote to all RTDs on 14 December 1984, informing them that it was hoped that 8Y would be available by April 1985.[407] The interim arrangements were to heat the existing product, which meant BPL would not meet the past issue level of NHS product.

234. Dr Lane stated in his Proof that from 14 December 1984, BPL no longer issued unheated factor VIII concentrate except at the specific request of a Transfusion Centre or Haemophilia Centre.[408] In the 5th draft of the Proof, he stated that 31 batches of unheated product were dispatched from July 1984 to April 1985, and three batches issued after 1 January 1985.[409] There was a note that this ought to be checked and confirmed with another source. This paragraph appears to be missing from the 6th draft.

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[403] Haemophilia Centre Directors Organisation, AIDS Advisory Document, HCDO0000270_007
[404] HCDO0000270_007, pg. 3
[405] HCDO0000270_007, pg. 3
[406] CBLA0000005_002, p.g.454-5 [1028]
[407] Letter from Mr Pettet to RTDs, 14 December 1984, CBLA0001955
[408] CBLA0000005_002, p.g.456 [1032]
[409] CBLA0000005_002, p.g.456 [1032]

1985

235. Heat-treated HL and 8CRV were issued from 1 February 1985.[410] 8Y became available from 1 April 1985 on a named patient basis, and only 8Y was issued after August 1985.

236. Dr Lane noted that in 1985, *"reservations amongst some clinicians as to the wisdom of using heat treated product still persisted"*, as there remained no satisfactory independent evidence that heat treatment at a particular level or duration worked for HIV, and there were lingering concerns that the heat treatment process itself might introduce unforeseen and detrimental changes in the product which would only manifest themselves at some later stage.[411]

237. On 24 January 1985, Dr Snape wrote a letter to Haemophilia Centre Directors, informing them of BPL's proposals regarding the supply of heated factor VIII concentrate and inviting them to make written requests for stocks of concentrate for use in the treatment of named patients.[412]

238. On 4 February 1985, Professor Bloom wrote to all Haemophilia Reference Centre Directors a letter which Dr Lane described as *"somewhat unfortunate"* and reflective of the fact that Professor Bloom had *"not properly read the material which we had sent out"*.[413] Professor Bloom's letter suggested that there were various alternative courses of action open regarding heated intermediate factor VIII and 8Y, when in reality, Dr Lane explained that they were already committed to producing as much heat-treated factor VIII intermediate concentrate as they could over the next few months but with the intention of introducing the demonstrably superior 8Y product as soon as practicable by scaling up production from April.

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[410] CBLA0000005_002, p.g.436 [980]
[411] CBLA0000005_002, pg.451. [1017]
[412] Letter from Dr Snape to all Haemophilia Centres, 24 January 1985, CBLA0001998
[413] CBLA0000005_002, p.g.461 [1045-6], referring to letter from Professor Bloom to all Haemophilia Reference Centre Directors, 4 February 1985, HCDO0000252_055

239. Dr Snape wrote to Haemophilia Centre and Regional Transfusion Centre Directors on 7 February 1985, indicating that the first despatches of heat-treated intermediate concentrate would be available in late February on a named patient basis.[414] He informed them that, due to thrombogenicity issues, heated factor IX concentrate would be subjected to extended safety testing, including assessment in a dog model, prior to release. He expected to be in a position to begin general issue in July.

240. On 28 February, Dr Snape wrote to Dr Duncan of the Medicines Division of the DOH, setting out the approach which BPL was adopting for the manufacture and issue of heat-treated factor VIII and factor IX for clinical use.[415] In his Proof, Dr Lane wrote, "*It was necessary to keep the Medicines Division advised of our approach both in relation to 8Y and the new heat treated factor IX since the approach we were adopting, and in particular the protocols which we would be using, would form, together with other information, the basis of licence applications for these products. We would normally advise of our approach, directly or through the DOH, of the protocols we would be using.*"[416] The timetable for factor VIII was set out in the letter as follows:[417]

a. 100 vials of HL(H) concentrate were issued to each Haemophilia Reference Centre in February 1985 for preliminary evaluation of safety and efficacy in named patients. The first reports had been received and indications were that the product was well tolerated.

b. General issue of HL(H) concentrate was to begin as soon as information from the preliminary evaluation had been assessed, which would probably be the first week in March. Issue would be to designated clinicians for the treatment of previously named patients, but via RTCs.

[414] Letter from Dr Snape to Haemophilia Centre Directors and RTDs, 7 February 1985, BPLL0001351_009
[415] Letter from Dr Snape to Dr Duncan, 28 February 1985, CBLA0002074
[416] CBLA0000005_002, p.g.463 [1051]
[417] CBLA0002074

c. Limited supplies of 8Y would then be issued to selected Haemophilia Centres for a trial of immediate safety and efficacy in named adult patients during the last week of February. Observations on responses were expected by mid-March.

d. Summarised results of the data would be made available to other Haemophilia Centres towards the end of March, and Directors would be invited to request a supply of 8Y for the treatment of named patients who met certain criteria.

e. An abridged licence application for 8Y product would be made in early May, after which, when stocks permitted, general distribution of 8Y would begin and HL(H) product would be phased out by the end of June.

241. Regarding factor IX, Dr Snape noted that their approach had been more conservative than North American fractionators, given their concern that heated factor IX concentrates should be free from potential thrombogenicity.[418] Although a small number of haemophilia B patients whose only recorded treatment was with NHS factor IX concentrate were known to be HTLV III antibody positive, Dr Snape emphasised their belief that their original assessment of comparative risks were probably reasonable. They intended to submit heated factor IX to extended testing in a dog model prior to clinical trial and therefore expected it to lag 2 to 3 months behind 8Y concentrate.

242. On 11 April 1985 Dr Smith sent Dr Lane a detailed report on the progress of heat treatment of factor IX.[419] In his Proof, Dr Lane explained that a slight delay had been caused by the discovery of a level of thrombin not revealed in the early stages, requiring an additional modification to the process.[420] He noted that the discovery of this problem at a late stage supported the decision to use dogs for testing before clinical trials.[421]

[418] CBLA0002074, pg. 3
[419] Memo from Dr Smith to Dr Lane and Dr Smith, 11 April 1985, CBLA0002489
[420] CBLA0000005_002, p.g.469-70 [1061]
[421] CBLA0000005_002, p.g.470 [1062]

243. On 16 April 1985, a PFL Working Party met to deal with heat-treated factor IX.[422] The meeting agreed that 50 u/L of AT III would be added to all batches, which would be heated at 80°C for 72 hours, allowing for clinical trials by the end of May or the beginning of June.

244. Dr Lane described the distribution arrangements for heat-treated factor VIII as "*not ideal*".[423] A letter from Mr Pettet to Dr French dated 2 May 1985 outlined some of the problems, including the slow response of Haemophilia Treatment Centres to BPL's request for lists of patients; by mid-March BPL had lists for just over 50% of centres.[424] By 1 April, the new ovens had been installed, leading to greater capacity and as a consequence, issue switched to a regional pro rata basis through RTCs.

245. In July 1985, Dr Smith prepared two papers, which Dr Lane noted were probably designed as briefing documents for the meeting of the Central Committee for Research and Development in Blood Transfusion which took place on 9 July 1985.[425] The first, "A new "Virus-Safer" factor VIII Concentrate of high specific activity", set out details about 8Y:[426]

a. The concentrate was at full scale production at BPL (1,200kg plasma) and yield was beginning to overtake that obtained from the less severely heated intermediate purity concentrate.

b. The immediate safety and efficacy of 8Y had been demonstrated by clinical trials.

c. Evidence for the reduction or elimination of viral transmission was being sought but several patients had already safely passed the point at which the first signs of NANBH transmission would have been expected.

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[422] PFL Working Party on Introduction of Heated factor IX, 16 April 1985, BPLL0011853
[423] CBLA0000005_002, p.g.471-72 [1067]
[424] Letter from Mr Pettett to Dr French (Consultant Haematologist, Queen's Medical Centre), 2 May 1985, CBLA0002154
[425] CBLA0000005_002, p.g.474 [1071]
[426] "A new "virus safer" factor VIII concentrate of high specific activity, CBLA0002205

246. The second paper, "factor IX Concentrate Heat-Treated to Inactivate Viruses" explained the following:[427]

a. Laboratory tests had shown that a small amount of thrombin was present in factor IX, and although the concentration produced was not thought to be physiologically significant, they had added a small amount of antithrombin III as a precaution.

b. The new concentrate 9A, dry heated after the addition of AT III, had been shown to be even less reactive than the parent 9D in the dog DIC model. Clinical trials of immediate safety and efficacy were planned to start in five Haemophilia Centres on 12 July 1985. Arrangements had been made to proceed to the treatment of patients susceptible to NANBH and HTLV III transmission in August.

247. A note of factor VIII issues dated 9 July 1985 showed that from January to July 1985, BPL issued 3.9m iu of unheated product and 4.3m iu of heated product.[428] A note on the 5th draft of Dr Lane's Proof added that these figures did not seem to tally with his statement that BPL only released heat treated product from January 1985 except when clinicians requested non-heat treated product, nor did it tally with the summary of batches showing only 3 issues of unheated batches from January to April 1985. It asked Dr Lane to confirm these figures.[429] This paragraph did not appear in the 6th draft.

248. In July 1985, an information sheet on 8Y was prepared by BPL and issued to Haemophilia Directors and RTDs.[430] It stated the following:

[427] "Factor IX concentrate heat-treated to inactivate viruses", CBLA0002206
[428] Factor VIII Table, 9 July 1985, CBLA0004260
[429] CBLA0000005_002, pg. 476, [1075]
[430] Note to Haemophilia Directors and RTDs enclosing "Information Sheet: July 1985", 24 July 1985, CBLA0002224

a. Factor 8Y would be issued through RTCs unless special provisions existed for product to be sent directly to the Haemophilia Centres. Allocations would observe the pro rata requirements except for the needs of clinical trials.

b. Until the new production unit at Elstree was completed, output of 8Y would meet about one third of current demand for concentrate, and so attempts had been made to define patients likely to benefit most from the security inherent in 8Y.

c. Haemophilia Centre Directors were being asked to compile lists of their patients considered "*at risk*".

249. An information sheet was produced in October 1985 which confirmed that from October, heat-treated factor IX concentrate would replace the previous product.[431] In his Proof, Dr Lane reflected that this marked "*the end of the rush to develop heat-treated NHS concentrates*", but work continued on refinements to the manufacturing process to increase the yield.[432]

Summary of Heat Treatment Claims

250. In response to an allegation that there was a failure to have sufficient regard to the pressing and urgent need to heat-treat factors VIII and IX concentrates from 1982, given (i) the ancient principle of pasteurisation; (ii) the risk with such concentrates of contamination by hepatitis and/or other viruses; and (iii) from mid-1982, the risk of HIV contamination with such concentrates, Dr Lane stated that:[433]

> "*1982 saw the earliest consideration being given to viral inactivation of factor VIII and IX concentrates. Heat treatment was merely one of a number of possibilities and when our research began in 1983, pasteurisation (or more correctly, heating*

[431] Information Sheet: October 1985 to Haemophilia Directors, CBLA0002274
[432] CBLA0000005_002, p.g.479 [1084]
[433] CBLA0000005_002, p.g.480-81[1086]

in solution) was indeed one method of heat treatment we considered, and we did so largely because it was an established method which had been applied to albumin. However, heat treatment was not itself the only possible method of inactivating virus, and it was right that we should consider the alternatives before committing ourselves to a particular line of research. In 1982/3 when the foundations for our research work were laid, it should be remembered that the risk being addressed consisted of the long-term potential [e]ffects in some patients of hepatitis Non-A Non-B infection. Although the MSC dates the HIV risk from mid-1982, this was really the earliest date that AIDS began to be appreciated and the dissemination of information regarding HIV did not lead to a tentative identification of the cause of AIDS as a virus until 1983. Confirmation of this in 1984 along with the news that the virus was heat labile places a different and more realistic perspective on events. The heat treatment of commercial products stemmed in the main from research done during the early 1980's which had nothing whatever to do with HIV at the time."

251. In response to the allegation that there was a failure, from 1982, either sufficiently or at all to require or commission and/or encourage and/or engage in research and development of heat treatment of domestically produced factors VIII and IX, Dr Lane stated that "*within the resources allocated (which were meagre), BPL and PFL accomplished a great deal producing ultimately the most successful of the factor VIII heat treated concentrates and an equally satisfactory heat treated factor IX concentrate.*"[434]

252. In response to the allegation that there was a failure, from 1982, to advise the DHSS and the Health Authorities to use heat-treated factors VIII and IX concentrates, given the risk of contamination with hepatitis and/or other viruses, Dr Lane stated that:[435]

"*It was no part of BPL/PFL's role to provide advice of this sort. Clinicians and public health laboratories and the regulatory authority had as much information as anyone throughout this period regarding the need for use of heat treated*

[434] CBLA0000005_002, p.g.481 [1087]
[435] CBLA0000005_002, p.g.481-2 [1088]

products. There was an understandable reluctance to embrace a new and unknown product and we could not possibly have stepped into the arena to offer advice regarding the use of products which we had not developed or subjected to any sort of clinical trial. Moreover, as shown by subsequent events, some of the heat treatment applied to commercial products did not work as far as HIV or hepatitis were concerned. Again, one has to bear in mind that the chronology is different from that presented in the MSC. The use of heat treated products did not appear to become an imperative until 1984 when HIV was positively identified as a virus. At this time, along with many other experts, I contributed to debates leading to the production of guidance notes for haemophilia clinicians. There were a number of Working Parties working on AIDS at any given time with representatives of the DOH and the Haemophilia Clinicians sitting on them and, in the circumstances, it seems a somewhat bizarre suggestion that BPL/PFL as manufacturers of product should have set themselves up as advisers on the treatment of patients. Lastly, on the subject of chronology, I would state again that by the time the commercial heat treated products became available, much, if not all of the damage had been done and severe haemophiliacs in particular were, in the main, already infected with HIV."

253. In response to the allegation that there was a failure, from 1982, to advise the Department of Health and the Health Authorities to use heat-treated factors VIII and IX concentrates, given the risk of contamination with hepatitis and/or other viruses and the additional risk of HIV contamination, Dr Lane stated that:[436]

"*I sat on a number of (but by no means all) expert groups considering, inter alia, hepatitis and later HIV. I contributed actively (drawing on my own experience and that of colleagues like Dr Smith) along with many other experts, to discussions at the various meetings of these groups which were all attended by representatives of the DOH and individuals who represented or had close links with the Health Authorities. The advice given by all concerned at these meetings led to a consensus*

[436] CBLA0000005_002, p.g.482-3 [1089]

as to what reaction there should be at any particular point and, in this sense, BPL/PFL contributed as far as it could and should to the advice which the DOH and the Health Authorities drew from a variety of sources before determining upon a particular course of action."

254. In response to the allegation that there was a failure to achieve domestic production of heat-treated factors VIII and IX concentrates, which should have been achieved by 1980 or such later time as may be justified on the evidence at trial, Dr Lane stated that:[437]

"*...our first heat treated products were available for trial in the spring of 1984. We were not put under pressure by haemophilia clinicians to provide more of this product. It was our own decision in the autumn of 1984 (on the back of the news that HIV was heat labile) that we unilaterally determined to switch to entirely heat treated factor VIII product; first our intermediate concentrates but subsequently our high purity 8Y products and to press forward as quickly as possible with our heat treated factor VIII research. Unless specifically requested to the contrary from February 1 onwards, we issued only heat treated factor VIII. The earliest point at which we could have issued heat treated product would have been in the spring of 1984 when we produced a few batches for trial use, but it should be remembered that, at this point, heat treated commercial concentrate was also available and that there was no limitation on the amounts which could be supplied had clinicians required it. The reality was that there were misgivings amongst clinicians at that time about the use of heat treated products. Some feared side [e]ffects, some that the heat treatment was not effective and that the balance lay in favour of continuing to use what was perceived to be the "safer", albeit unheated, NHS alternative."*

255. In response to the allegation that the DHSS having, in late 1984, announced that hone-produced factor VIII would be heat treated at BPL from 1985, the CBLA should have advised the Health Authorities to switch forthwith to imported heat-treated factors VIII and

[437] CBLA0000005_002, p.g.483 [1090]

IX concentrates in place of non-heat-treated product, and the CBLA should have forthwith invited and encouraged the Health Authorities to submit their existing stocks of concentrate to the BPL for testing and heat-treatment, Dr Lane stated that:[438]

> *"Advice... was indeed provided to clinicians/other interested parties regarding products used for treatment. In particular, advice was issued in December 1984 and represented the distillation of views of many experts, not just fractionators, but virologists as well as clinicians treating haemophiliacs. As to the recall of stocks of concentrate for testing and heat treatment, I have explained in my statement that, in relation to testing, there was no satisfactory test available at that time although product is routinely tested and confirmed by NIBSC. At the relevant time, we did not have the capacity to heat treat stocks of factor VIII retrospectively which might have been recalled. Additionally, unheated factor VIII produced by the NHS was still used by certain clinicians (conscious of all the risks involved), particularly in the treatment of those patients who were already sero-positive. Lasly, since we could not guarantee the integrity of products which had passed out of our control, the whole idea of retrospectively heat treating (even if this were feasible given our facilities at the time) was flawed. We had no idea under what conditions these products had been transported or stored and since we could not guarantee the safety of the product in vials which were recalled (and which we could not open to examine the contents without compromising the product), we would not have heat treated and re-issued it even if we had the facilities at the relevant time."*

256. Dr Lane's 5th draft Proof ends at this point. As already set out above, it was unsigned and undated and was never finalised.

JENNI RICHARDS QC, Counsel to the Inquiry

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[438] CBLA0000005_002, p.g.484 [1091]