[DRAFT NO 6 DATED 11TH DECEMBER 1990]

HIV HAEMOPHILIA LITIGATION

DRAFT PROOF OF EVIDENCE OF
RICHARD SPENCER LANE

I, RICHARD SPENCER LANE, M.B., B.S., M.D. (London), M.R.C.P., F.R.C. Path, WILL SAY as follows:-

1. I am the Director of the Bio Products Laboratory which changed its name from the Blood Products Laboratory on [ ]. Throughout my proof, I shall refer to it hereafter as the Blood Products Laboratory ("BPL"). I became Director in September 1978 (having been appointed Director designate with effect from 15th April 1977). In my capacity as Director, I am responsible for the day to day management of BPL and the Plasma Fractionation Laboratory ("PFL") and report to the Chief Executive (Mr. Bernard Crowley) and the Chairman (Mr. Ronald Wing) of the Central Blood Laboratories Authority ("CBLA") which has been responsible for the operation and management of BPL and PFL since 1st December 1982, and who are presently my employers.

2. I held various house appointments in paediatrics, medicine and surgery between 1959 and 1961, at which time I became Senior House Officer in pathology at the West Middlesex Hospital. Between 1962 and 1966, I was a research fellow

in haematology in the Department of Pathology, Royal Maternity and Samaritan Hospitals, Glasgow, and between 1966 and 1973, was employed as Scientific Officer at the Medical Research Council Experimental Haematology Unit at St. Mary's Hospital Medical School, London. From [ ] 1969 to [ ] 1970 I spent time as a 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, U.S.A. Between 1973 and 1975, I was lecturer in haematology at St. George's Hospital, London and between 1975 and the date I took up my appointment as Director designate at BPL, I was a Consultant Haematologist to the North East Thames Regional Blood Transfusion Centre, Brentwood in Essex.

3. I belong to the World Health Organisation Expert Advisory Panel on human blood products and related substances. I am a member of the International Society of Blood Transfusion ("ISBT") panel of experts on computerisation and automation in blood transfusion. I am a member of the Department of Health Advisory Group on Hepatitis and its Working Party on Anti-D and I am also a founder member of the British Blood Transfusion Society. I am also a member of the Department of Health Advisory Committee on the Viral Safety of Blood ("ACVSB").

4. For the purposes of my Proof of Evidence, it is perhaps sensible to distinguish the period up to 1977 from the period 1978 onwards. I was not of course employed at BPL until 15 April 1977 and, therefore, the comments set out in my Proof, insofar as they relate to most of the first period, are derived from an examination of the documents with the benefit of my background knowledge as a consultant haematologist working in the North East Thames Regional Blood Transfusion Centre. Throughout the second period, I was Director of BPL with the consequence that I have first hand knowledge of the events relevant to the issue of self-sufficiency.

I. INTRODUCTORY BACKGROUND

BPL

5. BPL has been established at Elstree since 1954 but I understand that its history goes back to 1943 when the Medical Research Council ("MRC") Blood Filtration Unit moved from the London County Council Laboratories at Carshalton to the Lister Institute of Preventative Medicine at Chelsea. With associated research on the preservation of human blood plasma and serum, large amounts of plasma were prepared for freeze-drying in the MRC plant at Cambridge serving military and civilian needs. Continuing under the joint management of the MRC and the Lister Institute on behalf of the Ministry of Health the title of the Filtration Unit was changed in 1946 to the MRC Blood Products Research Unit and the Unit pursued work which had already begun there on preparation of plasma fractions for clinical use. In addition, it continued the production of dried plasma in plants which were moved to Chelsea and Elstree following the closure of the Cambridge Unit.

6. Between 1954 and the commissioning during 1987/1988 of the present, much extended, manufacturing facility, the Laboratory at Elstree underwent successive development to increase production of freeze-dried plasma to meet post-war National Health Service needs and enlarge facilities for plasma fractionation. It was managed on a day to day basis by the Lister Institute for the Ministry of Health (as it then was) which provided financial support for its operations through the agency of the MRC. The Lister Institute held the lease for the main site at Elstree.

7. Throughout its operations, BPL has been maintained and developed by direct financial support from the Ministry of Health (later the Department of Health and Social Security and now the Department of Health, collectively referred to hereafter as "DOH"). However, throughout its involvement with BPL, the Lister Institute acted as the employing authority for the staff working at BPL. Management of BPL was a complex affair involving the MRC who, on behalf of the DOH, maintained responsibility for policy, budgetary approval, planning and building developments, etc., until the early 1970's. Thus an extension to BPL which was commissioned in 1962 was controlled by the MRC.

8. Growth and requirements for blood products arising from the development of new fractions, plasma protein fraction and dried antihaemophilic globulin (AHG or Factor VIII), resulted in the need for a further extension of BPL which commenced planning in 1965 and was commissioned as a new Large Fractions wing to the complex that already existed in 1972. By about this time, the MRC's role in management was diminishing as production became the dominant purpose for the facility replacing the earlier research based laboratory. The 1972 extension was built with the Lister Institute acting as the client body for the purpose of the building operation on behalf of the DOH. In 1975, the Lister Institute took over full responsibility for the administration of BPL on behalf of the DOH.

9. Within months of completion of the 1972 extension, the need for a further extension to the BPL facilities became evident. Pressures of under capacity coupled with outdated concepts of production enshrined in earlier building designs pointed to a completely new building being required. A vital and preliminary need was for a pilot process laboratory to examine new technology and process methods, outside main production. Plans were first submitted in 1975 but, although the need was strongly supported, in the event, approval in principle for a pilot laboratory was not given until 1990 by the DOH.

10. In September 1978 for commercial reasons, the Lister Institute ceased operations at Elstree. After realising its capital resources, the Institute returned to the support of basic research through a newly constituted trust body.

11. The closure of the Institute had immediate and far reaching consequences for BPL, and a series of significant events followed rapidly. The North West Thames Regional Health Authority ("NWT") met the interim need to take over as the legal employing Authority on behalf of the DOH. To secure BPL at Elstree, the DOH negotiated the acquisition of the whole Elstree site and buildings from the Lister Institute and completion of this acquisition took place during September 1979, the existing leasehold reverting back to the DOH. The acquisition of the land which surrounded the very small site on which BPL had been located removed a primary spacial constraint on the extension and redevelopment of BPL.

12. The management of BPL also altered in that the DOH and NWT now handled policy, planning and financial affairs through a Joint Management Committee ("JMC") for the DOH and had its first meeting on the 13th December 1978. With this new management group, came the conclusion of the existing advisory management body which was called the Advisory Sub-Committee on Blood Products and Blood Group Reference Laboratories of the Central Committee of the National Blood Transfusion Service. The JMC was further assisted by the formation of a Scientific and Technical Committee, and the Finance Sub-Committee, which were both set up during 1979.

13. The first Director of BPL, Dr. (later Sir William) Maycock, retired (in September 1978), and I replaced him as Director of BPL.

14. Shortly after I became Director of BPL, the Medicines Inspectorate carried out a detailed inspection of the BPL facility in April 1979 (and subsequently the PFL facility), and reported that the Laboratory was seriously sub-standard as a pharmaceutical manufacturing factory. There followed a period of uncertainty during which basic and essential up-grading which had been planned prior to the Medicines Inspectorate visit was postponed, re-planned, modified and then approved prior to 1982, at which time CBLA took over responsibility for BPL and PFL, and before the DOH approved the building of a completely new manufacturing facility which, after certain difficulties, was eventually commissioned during 1987/1988.

PFL

15. I refer to the proof of evidence of Dr. J.K. Smith for further detail regarding the history of the PFL located at Oxford.

16. In the decade leading up to 1964, Professor R.G. Macfarlane and Dr. Rosemary Biggs developed a unit in Oxford with special expertise in blood coagulation. The unit developed a world reputation in haemophilia diagnosis and treatment. In 1964, Professor Macfarlane proposed that a Haemophilia Centre should be set up on the Churchill Hospital site in Oxford and that this should comprise a Coagulation Research Unit administered by the MRC, a clinical unit administered by the Oxford Hospital Board of Governors, and a laboratory for the fractionation of plasma which was to become PFL. Because of similarities with BPL, it was proposed that BPL should manage PFL on behalf of the Lister Institute.

17. New premises on the Churchill Hospital site were completed in 1967, and PFL was managed by Dr. Ethel Bidwell, a leading scientist who worked in Dr. Biggs' unit, and under the overall directorship of Dr. Maycock who was already administering the BPL. As with BPL, the funding of PFL was provided directly by the DOH.

18. These arrangements lasted until the closure of the Lister Institute in 1978 and over this period the PFL made a major contribution to the production of freeze-dried Factor VIII for the treatment of haemophilia A, and Factor IX for the treatment of the related disorder haemophilia B. Dr. Bidwell retired in 1981 having worked, together with myself, to rationalise activities at BPL and PFL. Following the commissioning of BPL's new production facility by 1988, the role of PFL has changed to provide pilot process capability in the continuing absence of a similar facility at Elstree. The Oxford Haemophilia Centre ("OHC") developed in parallel with PFL (and much of PFL's product has been directed to OHC), has thrived and is the largest Centre for the treatment of haemophiliacs in England and Wales.

CBLA

19. Both BPL and PFL together with the Blood Group Reference Laboratory ("BGRL") (whose activities are not relevant for present purposes) have, since 1st December 1982, been the responsibility of the CBLA. The CBLA presently comprises members who are as follows:-

Chairman: **Mr. Ronald A. Wing, CBE FPS.**
A member of the East Yorkshire Health Authority, Past Chairman of Sanoffi, a pharmaceutical company. Recent past President of the Association of British Pharmaceutical Industries.

Vice Chairman: **Sir Vernon Seccombe, JP**
Past Chairman of the South Western Regional Health Authority.
Retired Electrical Contractor.

Members: **Mr. Roderick Braithwaite.**
A Management Consultant.

Dr. Brian W. Cromie.
Retired Chairman of Hoechst Pharmaceuticals U.K.
Retired Chairman of Arthur Cox Pharmaceuticals.
Chairman of Waverley Pharmaceuticals and a Director of Charter House Venture Fund Management Ltd. He has also served on the Medical Commission and the ABPI.

Mr. Hamilton Dempsey, FPS.
Chairman of Advertising and Design Associates.

Dr. Peter Kernoff.
Director of the Haemophilia Reference Centre at the Royal Free Hospital and School of Medicine.

Miss Katherine Mellor.
A partner of Elliot & Co and past President of the Manchester Law Society.

Mr. Colin Walker, OBE.
Chairman of East Anglia Regional Health Authority.
Managing Director of a farming company.

20. Under the Chairmanship of Mr. R. Wing the Senior Executives responsible for the day to day management of BPL and PFL are as follows:-

Mr. B. Crowley:	Chief Executive
Dr. R. Lane:	Director of Operations
Mr. B. Savery:	Director of Finance and Administration

Dr. T. Snape is Factory Manager.

21. The staff of BPL number approximately 380 and in the case of PFL about 30.

22. The first Chairman of the CBLA was Mr. R. D. Smart, who came to the CBLA with experience in pharmaceutical manufacturing: until 1982, he was the

Commercial Director of Glaxo Holdings Limited. The then Secretary of State for Social Services, Mr. Norman Fowler wrote to Mr. Smart on 17th November 1982 (document no. 1569) setting out the CBLA's task which was to provide an effective management body for the three Central Blood Laboratories - the BGRL, the BPL and the PFL. The Central Blood Laboratories Authority (Establishment and Constitution) Order 1982 ("the 1982 Order") (Appendix 1) specifies the main functions of the CBLA. CBLA was established as a Special Health Authority and was to perform on behalf of the Secretary of State the functions specified below and such other functions as the Secretary of State might direct the CBLA to perform on his behalf:-

"(a) The provision of laboratories for the manufacture of blood products and other purposes;

(b) The preparation of plasma fractions for therapeutic, diagnostic and other purposes;

(c) Research and development in plasma protein fractionation and for other purposes;

(d) The manufacture of blood grouping reagents and other related reagents."

23. The various Committees established by the CBLA to deal with specific aspects of the management of BPL/PFL are outlined in Appendix 2.

THE NATIONAL BLOOD TRANSFUSION SERVICE ("NBTS")

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24. This was constituted in 1946 from an amalgamation of the emergency transfusion services during the 1939-45 war. Initially the NBTS was centrally administered. In 1948 administration was delegated to the Regional Hospital Boards as part of the hospital and specialist services provided under Section 3 of the National Health Service Act 1946. There are 14 Regional Transfusion Centres (RTC's) in England and Wales (one in each Region except the South East and the South West Thames Region which is served by one Centre). Some regions have sub-centres. The RTC's in England are administered by the Regional Health Authorities ("RHA's") and financed by RHA's from the Regional financial allocation from the DOH. In Wales the transfusion service is administered by a District Health Authority ("DHA") on behalf of the Welsh Office.

25. Each RTC has a medically qualified consultant as a Director who is responsible to the RHA or DHA for blood transfusion services. The Director has supporting consultant and other medical staff, a lay administration and specialist staff for donor organisation, nursing and for the provision of laboratory services.

26. The corner stone of the NBTS has always been voluntary blood donors. In 1977, there were approximately 2.5m. donors on panels maintained at RTC's. At present the number is 2 million. A significant reduction in donors has followed the concern about AIDS. This is also a feature in other European countries, e.g. France. Although the NBTS underwent considerable functional changes over the period from its inception, throughout the period which is relevant to this litigation the organisation changed relatively little. It was, in effect, a loose confederation of 14 RTC's, regionally financed, which varied considerably from region to region and were neither controlled nor financed in the same way as BPL/PFL. There were effectively four links with the DOH:-

(a) There was a part-time Consultant Adviser on Blood Transfusion to the DOH.

(b) There were periodic (about 5/6 times a year) meetings of Regional Transfusion Directors. This "body" was not constituted statutorily. The meeting carried no executive function and although its purpose was, in part, to advise the Consultant Adviser, it served as an unofficial, informal mechanism for exchange of information between constituent units of the NBTS and the DOH.

(c) A Central Committee for the NBTS was formed by the DOH on the recommendation of the Committee on the Future of the NBTS (1974) (the Reid Committee), which proposed terms of reference and the constitution of the Central Committee both of which were accepted by the DOH.

The terms of reference were:-

> "To keep under review, the operation of the National Blood Transfusion Service, including the Blood Products Laboratory and the Blood Group Reference Laboratory, in England and Wales and to advise the Department of Health and Social Security and the Welsh Office on the development of the service."

The part-time Consultant Adviser and two elected Regional Transfusion Directors were members of this Committee. The Committee included representatives nominated by the Royal College

and other members in various specialities of medicine. The Chairman was the Deputy Chief Medical Officer of the DOH.

(d) There were regular meetings of the Regional donor organisers under the chairmanship of a senior administrator of the DOH. This particular Committee existed largely to review publicity material for blood donor recruitment, since much of this material, which was of a high quality, was produced separately by the DOH in conjunction with the Central Office for Information ("COI").

27. I think it is fair to say (and indeed this is summarised in a memorandum which was produced in June 1977 as a submission to the Royal Commission on the NHS (document no. 554)) that the organisation which existed within the Transfusion Service during the period which is relevant to this litigation, limited the development of the national aspects of the service. The RTC's were poorly represented centrally as described above, and the Central Committee itself was only an advisory committee to the DOH and, on national or any other aspects of the Transfusion Service, the DOH was not (for procedural reasons) able to instruct Regions on the allocation of finance to RTC's. The RHA's were not necessarily involved in national policy-making for the NBTS, although central policies might require RHA's to commit allocations of extra funds from Regional budgets to finance development at RTC's.

28. Notwithstanding the submission, the problems identified in it persisted, and it was only in 1988 that a National Directorate for the NBTS was established, reporting to the Director of Operations of the NHS Executive Committee. The National Directorate remains only advisory and without regional executive authority.

HAEMOPHILIA

29. The term haemophilia characterises a group of conditions which have mainly a genetic basis and which result in a tendency to abnormal bleeding. Bleeding may be severe and be life threatening or cause severe morbidity. The bleeding is caused by a reduction in plasma levels of certain specific proteins which assist in the normal process of blood clotting. There are two main types, haemophilia A and B where the deficient proteins are Factor VIII and Factor IX respectively.

30. Haemophilia was described as abnormal bleeding in families in the 2nd century but the main defect was not characterised until nearly 100 years ago. Haemophilia B was not described as a separate condition until 1952. The clinical symptoms of haemophilia A and B are similar.

31. Both haemophilia A and B are genetically sex-linked recessive bleeding disorders. The incidence of haemophilia is approximately 1 : 10,000 of the worldwide population, of which some 20% is of the haemophilia B type. Female haemophilia is extremely rare and probably represents marked expression of the carrier state. The genetic state may arise by spontaneous mutation in an estimated 30% of new cases.

32. The frequency and severity of bleeding in haemophilia may be predicted from the level of clotting factor in the plasma. Less than 1% of normal clotting activity may be associated with severe and frequent bleeding which occurs internally in many sites: however, the crippling effects of repeated bleeding into joints and muscles is a characteristic of the condition.

33. The control of bleeding by blood transfusion was demonstrated in 1840 but until 1964, when the preparation of cryoprecipitate was first described, effective treatment was limited by volume restrictions imposed by blood or whole plasma transfusion. During the past twenty years, successive improvements in the large scale preparation of purified potent freeze dried concentrates of Factor VIII and Factor IX have made the control of abnormal haemophiliac bleeding both more effective and safe. Whereas, untreated, a severe haemophiliac could have expected death or severe disability by the end of the third decade, new haemophiliacs can now anticipate a controlled active life of near normal length without unacceptable periods of hospitalisation.

34. Improved treatment has been paralleled by better diagnostic means and clinical management. The future holds the potential benefits of recombinant DNA-produced clotting factors and the possibility of gene-replacement.

COAGULATION FACTORS: PREPARATION AND USE

35. BPL/PFL only fractionate plasma collected by the fourteen Regional Blood Transfusion Centres in England and Wales. Blood consists of a cellular component in an aqueous solution of proteins and salts known as "plasma". Blood is donated either as whole blood or as plasma collected by means of plasmapheresis. In plasmapheresis, the donor's plasma and red cells are separated at the time of donation and the red cells returned to the donor during the process of donation. Plasmapheresis enables the donor to safely donate more plasma than can be obtained from whole blood donation. UK practice permits a regular blood donor to donate up to three donations of whole blood a year. In contrast, up to 12 litres of plasma (approximately 20 donations) may be given in a year by plasmapheresis because the donor retains the red cells.

36. The raw material for BPL and PFL comprises outdated plasma from blood which has exceeded its shelf life of up to 35 days and Fresh Frozen Plasma ("FFP") which constitutes over 95% of source materials for fractionation. For the purpose of manufacturing Factor VIII and Factor IX only FFP can be used. Factor VIII and Factor IX concentrates produced from FFP by BPL/PFL and commercial manufacturers, were not the only method of treatment for haemophiliacs. Particularly during the 1970's and now, in exceptional circumstances, cryoprecipitate has provided an alternative treatment. Indeed this was the principal product used to treat haemophiliacs for a long time. BPL/PFL have never produced cryoprecipitate for treating haemophilia patients. This has always been produced by Blood Transfusion Centres. Cryoprecipitate is produced by freezing and the controlled thawing of plasma and, as I describe below, forms part of the fractionation process generally employed in the purification of Factor VIII concentrate.

37. In contrast to the treatment of haemophilia using plasma transfusions or infusions of cryoprecipitate where, for reasons of injection volume, the product of only one or a small number of donors could be used to treat a patient, the manufacture of concentrates involves the pooling of FFP necessary for the efficient separation of the various proteins in the plasma. The concentrates of coagulation factors prepared from large plasma pools have the advantage of batch consistency and assayed potency.

38. In fact the fractionation process used to produce Factors VIII and IX, was not geared solely to production of these two factors, but enabled BPL and PFL to produce, from the same pool of plasma being fractionated, a number of other products which like Factors VIII and IX, were made available to the NHS for treatment of patients. At all material times, freeze-dried Factors VIII and IX

concentrates together with immunoglobulin and albumin were the principal products produced by BPL and PFL.

39. Up to 1978, the intermediate Factor VIII concentrate produced at BPL was coded 8IP and from 1978 to 1985 was re-coded HL. During this latter period the equivalent product at PFL was coded 8CRV ("cooled reduced volume"). The intermediate concentrate freeze-dried Factor IX was coded 9D. These intermediate purity products were replaced by high purity freeze-dried heat treated Factor VIII concentrate called 8Y and freeze-dried heat treated Factor IX concentrate coded 9A in 1985.

40. The change which the availability of freeze-dried Factors VIII and IX concentrates brought in the treatment of haemophiliacs became marked during the 1970's. In the early part of the decade, cryoprecipitate was used in the majority of cases for the symptomatic or elective treatment of bleeding. Gradually as the scale of freeze-dried Factor VIII concentrate production at BPL and PFL increased through the 1970's augmented over the same period by the importation of similar products from commercial manufacturers in the United States, the demands of haemophilia care rapidly increased the forecast for national use of concentrates. In particular, it enabled severe haemophiliacs to lead near normal lives by using Factor VIII concentrate in a prophylactic manner to prevent the occurrence of bleeding.

41. Neither Factor VIII nor Factor IX were without risk. From the beginning, it was known that blood and its derivates - plasma, cryoprecipitate and concentrates were sources of hepatitis B virus transmission. Additionally, Factor IX gave rise to problems from veinous thrombosis in a small minority of patients. Towards the end of the 1970's, it became clear that there were other types of hepatitis virus which both plasma and plasma products could transmit. In

a small proportion of patients Factor VIII and Factor IX were neutralised by antibodies (immune inhibitors to the infused protein). That said, the risk of fatality resulting from the use of the products prior to the discovery of HIV was low, and the risk-benefit ratio was clearly in favour of their use, for without them, in severe and moderately affected haemophiliacs early fatality was common and morbidity was severe.

42. The fractionation process is complex and I would refer to the Statement of Dr. J.K. Smith for a detailed description of the work carried out on the processes currently in use at BPL/PFL. Appendix 3 sets out a diagrammatic representation of the process of manufacturing HL or 8CRV which may be simply described as follows below.

43. Plasma separated from whole blood by centrifugation or by plasmapheresis is not sterile but is collected aseptically into closed sterile containers. Blood Transfusion Centres are required to test all plasma to exclude markers for hepatitis B virus and for antibody to HIV 1: this is standard procedure throughout the NBTS which has been extended as from June 1st 1990 to include the marker for antibody to HIV II. In accordance with specifications, tested plasma found non-reactive to the above viral markers, is frozen to -40°C and, with appropriate documentation, is despatched in the frozen condition to BPL or PFL.

GAP

44. FFP is currently collected and transported in single donation containers (although previously, tested plasma was pooled into 5 litre containers prior to freezing and despatched to BPL/PFL). Plasma is maintained frozen at the Fractionation Centres in documented quarantine for a minimum of three months before use.

45. At the start of fractionation, donations of frozen plasma constituting a batch of up to 3,400 kilos or 3.4 tonnes are removed from containers, crushed,

thawed and pooled. Batch size has increased from 100 kilos (in the mid-1970's) to the current level above. There are on average 3½ donations per kilo. Accordingly some 15,000 plasma donations may be represented in a defined batch of product.

46. Plasma is thawed to 0°C. and at this temperature some protein stays in suspension and can be removed by centrifugation. This protein fraction is cryoprecipitate. The process of cryoprecipitation concentrates the Factor VIII. Cryoprecipitate is re-dissolved and unwanted proteins are removed by additional purification steps, leaving highly purified Factor VIII in a condition suitable for final formulation.

47. The proteins left in solution after cryoprecipitation include Factor IX which can be removed selectively by its adherence to a solid phase resin. Further treatment of the resin releases a purified Factor IX in a form suitable for final formulation.

48. After final formulation, both Factor VIII and Factor IX are made bacteriologically sterile by filtration, undertaken in pharmaceutically controlled operation facilities. The filtered product, after being filled into vials, is freeze-dried by a process known as lyophilization. Following lyophilization the vials are closed and sealed.

49. Since 1985 both Factor VIII and Factor IX freeze-dried products have been subjected to heat treatment in the dry state at 80°C for 72 hours which are conditions shown by clinical use to inactivate hepatitis and human immuno deficiency viruses.

50. Plasma pools, intermediate products and final products are required to be tested for markers for hepatitis B and antibody to HIV 1 at the Fractionation Laboratories and by the National Institute of Biological Standards and Control ("NIBSC"). After testing, the vials are inspected and packed. After release by the Quality Department and NIBSC, products are distributed to Regional Transfusion Centres.

BATCH MANUFACTURING RECORDS

[THIS SECTION IS TO BE CHECKED BY DR SNAPE/DAVID DONALD]

[51. I refer to the Proof of Evidence of Dr T J Snape, Production Manager of BPL. For the sake of completeness I will provide below an over-view of the incident system.

52. Incident records of one sort or another have been maintained by BPL since 1980. Since 1987 these have followed a formal procedure but in earlier years they were more informal and could vary from one to another. All incidents have been, primarily, handled by the QC department [is this true?] with Dr Snape or his predecessor reporting directly to me both during the compilation of an incident file and at its closure. Other departments within BPL and PFL are involved in each incident to a lesser or greater extent, as is the PHLS.

53. Incident files are opened whenever BPL product is or might be involved in either:

a. a donor related incident ie where a donor is found to be HIV positive by an RTC and has donated before, or

b. a product related incident, ie when the treatment records of a patient who seroconverts show BPL product has been administered during the period when infection is possible.

The type of incident can be deduced from the incident numbers prefix. If it is a donor incident it will be an RTC code from this list:

N = Newcastle

S = Sussex

U = Wales

K = Mersey

V = Lewisham

M = Manchester

J = Brentwood

W = Edgware

D = Trent

P = Tooting

F = Oxford

ST = St Thomas

T = Bristol

RF = Royal Free

H = Birmingham

C = Yorkshire

G = Cambridge

GOS = Great Ormond St

LonH = London Hospital

UCH = University College Hospital

U of W = University of Wales

R Vic = Royal Victoria Hospital

LMT = Lord Mayor Treloar

Where a product is implied by analysis of medical records at PHLS the prefix is PR. The following two digits show the year and the number which follows is taken from the numerical sequence within that year.

54. Upon notification of an incident the Head of QC will immediately decide whether recall of product is warranted. In some cases a donor incident may arise years after previous donations were processed into product, in such circumstances recall is pointless. In other cases the product may still be in process or only recently despatched in which case all possible steps will be urgently taken to recover the vials. The Haemophilia Centres who have been supplied will be told immediately and they will set about recovering the AHF, passing the word both to clinicians who hold stocks and to patients on home treatment. If part of the batch has been used the co-operation of clinicians will be sought to carry out a follow-up of those patients treated.

55. In addition to the identified batch into which the suspect donation was added other batches which were closely associated with it may be investigated. Such a batch would be a co-dried batch which could, conceivably, become infected.

56. Obviously some batches were processed and issued months or years before the incident arose. Any product in clinicians possession has, in such a case, either been used or is time expired. Steps are still taken to recover such product. Other departments within BPL often hold product for one reason or another and these are also notified of any incidents relating to batches in their possession.

57. Where a donor related incident is notified which connects with heated or tested product the only follow up is to confirm that the incident is not related to a reported seroconversion of a patient. Thus far no such incident has implied that heated and tested product could carry an infection. If it were shown, even circumstantially, that such a product could be compromised it would be immediately withdrawn and follow-up checks by clinicians initiated.

58. Since testing for HIV has been carried out at BPL and all RTC's there have been (No) of positive tests on incoming plasma. Testing after heat treatment has uncovered (No) of infected batches. There have been no product incidents relating to heated and tested AHF (either Factor VIII or IX).

HEPATITIS

59. Hepatitis presents in acute, sub-acute and chronic forms. With hepatitis B and C the acute form may be severe and fulminant resulting in death. Sub-acute and chronic hepatitis may be life-shortening in haemophiliacs although the records of fatalities indicate hepatitis as a cause of death in only a minority of the total recorded deaths. By way of illustration, a paper reprinted from the British Medical Journal, 19 March 1983 by C.R. Rizza and Rosemary J.D. Spooner records the causes of death in patients with haemophilia A and haemophilia B over the period 1976-1980 (see miniprint table Vm on page 8 of document no. 1617). Cerebral haemorrhage was the commonest cause of death in haemophilia A patients, accounting for 26 of the 89 deaths. Hepatitis was recorded as the cause of death in one patient with haemophilia A and one with haemophilia B (although the type of hepatitis is not specified). The longer expected survival of haemophiliac patients introduces a higher clinical significance to the chronic disorder. On page 5 of the same paper, median life expectancy was 69.1 years for severely affected haemophiliacs, as compared with 72.8 for normal males.

(The paper notes, however, that these figures should be treated with caution: the numbers in the calculations were relatively small and it was possible that deaths may not all be reported to Haemophilia Centre Directors).

Hepatitis A:

60. This is sometimes called acute infectious hepatitis. Its transmission is not customarily considered as a transfusion transmitted form of hepatitis although there are published reports of rare associated cases in patient recipients of blood. The viral infection is through the enteral (intestinal) route usually from faecal contamination of water or food. The infection is often sub-clinical i.e. it is without symptoms, particularly in the young: otherwise symptoms may be mild and associated with abdominal discomfort. The duration of infectivity of the patient is uncertain but is probably from 7 to 14 days before to seven days after the onset of jaundice. Treatment in the majority of cases is symptomatic. The prognosis is good and patients make a satisfactory recovery associated with immunity against further infection.

Hepatitis B:

61. This is also called serum hepatitis. It has an incubation period which may be up to six months, but is commonly 10 to 16 weeks after infection. It is transmitted parenterally and sexually and at birth in the case of the infected mother. Therefore it is transmitted by transfusion of infected blood and blood products manufactured from such blood, or by the use of contaminated syringes or needles. It is therefore a disease associated with parenteral addiction. Hepatitis B is a serious disease. It carries published mortality rates between 2% and 5% and after the acute infection may be associated with the development of chronic liver disease and association with the hepatitis D (delta) virus and an associated

increase in hepato-cellular carcinoma. Recovery from the disease is most frequently associated with development of immunity although a small percentage of patients retain carrier status (approximately 0.1% in the UK but up to 5% in Asiatics) and are capable of transmitting the disease by any of the above routes.

62. The presence of hepatitis B infection may be associated with a number of viral markers. At the onset of infection the patient's serum may be found to contain actual virions or virus particles known as core particles (Dane particles). Associated with core particles are various amounts of surface antigen (abbreviated as HBsAg). In the majority of patients the early immune response follows the viraemia and may demonstrate all or some of the following features: the presence of antibody to the core antigen; to e-antigen which is core associated; and against HBsAg. It is generally considered that the absence of antigen and the presence of antibody to HBsAg reflects recovery from infection and non infective status.

63. The Transfusion Service and blood product manufacturers test all donors/donations/plasma pools/finished products for HBsAg by an approved third generation test. Tests used by the Transfusion Service and BPL/PFL since the start of the 1970's are described in Appendix 7.

Hepatitis Non-A Non-B:

64. This expression is thought to include a group of viruses which may be transmitted by both enteral and parenteral routes. Within this group the recently described hepatitis E virus is transmitted in a similar manner to hepatitis A and is a reported cause of epidemic hepatitis particularly in Asian countries. Although not yet visualised, a virus now described as hepatitis C (HCV) has been defined through its presumed genomic structure: this virus probably accounts for greater

than 70% of parenterally transmitted Non-A Non-B (HCV) infection associated with the transfusion of blood and blood products. Most recent published information suggests the presence of hepatitis C antibody in the normal population of 0.5% to 2% but levels up to 6% to 10% in high risk groups e.g. addicts.

65. The result of initial infection is most frequently sub-clinical. However, there may be a mild acute illness associated with abdominal discomfort and slight jaundice and in rare cases a fulminant hepatitis similar to that of hepatitis B, may result in death. The more significant feature of HCV infection is the progression in a percentage of patients (possibly up to 50%) of sub-acute and chronic forms of hepatitis which may be life shortening.

66. Following the reduction in transmission of hepatitis B as a result of effective donor screening during the 1970's and early 1980's, Non-A Non-B hepatitis emerged as the dominant form of transfusion associated hepatitis. The true rate of transmission following blood transfusion in the UK has yet to be reliably determined. However, blood products prepared from large plasma pools have accounted for viral infection in most treated haemophiliacs. Factor VIII prepared from commercially collected donor plasma had an early association with HCV transmission because it caused an acute clinical condition in many patients. However, the use of liver function tests (alanine aminotranspherase "ALT") in all haemophiliacs had shown by the early 1980's that virus transmission occurred with Factor VIII prepared from voluntary donor blood sources, although these products did not produce an acute illness in more than a small percentage of patients. Most recent information indicates an order of magnitude more virus donors in the commercial donor population than in the voluntary donor population, thus accounting for a higher viral load in plasma pools and finished products with the possible resultant increase in overt acute infection.

67. Clinical, epidemiological and experimental studies in laboratories, have indicated that Non-A Non-B hepatitis may be caused by two and possibly more than two infectious agents. Clinical evidence is based on the observation of multiple attacks of hepatitis in individual patients. Epidemiologically, short incubation (2 to 5 weeks) and long incubation (5 to 10 weeks or longer) forms of Non-A Non-B hepatitis have been described. The incubation period, however, does not appear to be a reliable index for differentiating between the two Non-A Non-B types of hepatitis, and the differences in the incubation period may represent differences in viral dose or patients' susceptibility to infection.

HIV

68. It is currently believed that two strains of the HIV virus (HIV 1 and HIV II) are responsible for human immunodeficiency syndrome, AIDS. We are presently concerned with HIV 1. HIV II is a rarer variant.

69. HIV infection can be transmitted in blood, plasma, seminal fluid, and vaginal secretions, although there does not appear to be a sufficiently high level of the virus present to enable it to be transmitted by tears and saliva. HIV infection can therefore be transmitted by the injection of contaminated blood or blood products.

70. HIV can also be transmitted by heterosexual and homosexual contact and drug abuse.

71. Once the virus has entered the host's system, it binds to the specific cell receptor (CD4) which is present on T lymphocytes and other cells in the immune system. The virus enters the lymphocytes and under certain conditions which are

still not completely understood, will result in a significant reduction in their numbers.

72. A decline in the CD4 or T cell sub-set will cause a reduction in cell-mediated immunity and in other functions concerned with modifying and controlling the production of antibodies.

73. The host usually develops antibodies to the virus (known as seroconversion) although the effect of these antibodies on viral replication is not clear.

74. It is believed that the period between infection with HIV and seroconversion is in the region of three months but it may exceed this time in some individuals. However, after seroconversion, the virus can stay quiescent in infected cells for a period of months/years. A variable period of time may elapse between HIV infection and the development of clinically overt acquired immune deficiency syndrome or its clinical precursors. It is not yet understood what factors may precipitate the rapid increase in viral replication leading to the profound decline in the immune competence of the host.

75. The initial infection by HIV virus may be accompanied by a mild glandular fever like illness. The onset of overt AIDS may be preceded by an intermediate stage of immunological abnormalities, described collectively as AIDS Related Complex ("ARC"). AIDS is characterised by opportunistic infections and increased susceptibility to certain malignant conditions: current methods of drug treatment appear to give a measure of symptomatic relief, but this is transient and early death is the usual outcome.

II. THE PLAINTIFFS' CLAIMS

76. The claims advanced in the Re-Amended Main Statement of Claim ("MSC") against CBLA are grouped under five headings, vis:-

(a) Self-Sufficiency and the Blood Transfusion Service;

(b) Manufacture of Non-Heat-Treated Concentrates;

(c) Heat Treatment;

(d) Hepatitis Risk and/or Risk of Other Viral Infections;

(e) AIDS Risk.

77. It may be convenient for the purpose of this proof of evidence to deal with each heading and the allegations grouped under it in turn. I have, however, dealt with non-heat treated concentrates and heat treatment under the one heading "Heat Treatment and Manufacture of Non-heat-treated Concentrates".

SELF-SUFFICIENCY AND THE BLOOD TRANSFUSION SERVICE

[NB: SUBEJCT TO RE-RE-AMENDMENT BY THE PLAINTIFFS]

OVERVIEW

78. The Plaintiffs contend that once the objective of self-sufficiency in blood products had been established it was the duty of the BPL to advise the DOH and the Health Authorities of ways of fulfilling the objective to the extent that BPL was unable to manufacture sufficient Factor VIII. It is contended that CBLA should have [sent plasma collected in England and Wales to Scotland and/or commercial manufacturers for fractionation] and should have made suitable efforts to encourage plasma production by the NBTS. [NB: THIS ASPECT OF THE CASE IS STILL SUBJECT TO REVIEW BY THE PLAINTIFFS].

79. In essence, the Plaintiffs argue that plasma collected in England and Wales was intrinsically safer (in terms of its potential to transmit virus), than plasma collected from paid donors: if the supply of plasma to the BPL were boosted, fewer haemophiliacs would have required imported commercial Factor VIII concentrate which carried a higher risk of contamination with HIV.

80. Throughout the 1970's and 1980's, England and Wales was self-sufficient in relation to Factor IX, since the demand for this product, used to treat haemophilia B patients, was much lower reflecting the lower incidence of this form of haemophilia.

81. The data that has emerged with regard to the relative extent of HIV infection amongst haemophilia B sufferers treated exclusively with NHS Factor IX produced by BPL/PFL suggests that pro rata there was a lower incidence of infection when compared with the rate of infection of haemophilia A sufferers who used commercial U.S. Factor VIII concentrate. So far as we are aware, there is little difference between Factor VIII and Factor IX in terms of their inherent potential to transmit HIV when manufactured from infected donations of plasma, and the quantity of Factor IX required to treat severe haemophilia B sufferers is comparable with the quantity of Factor VIII used by haemophilia A sufferers. Nevertheless, the pro rata incidence of HIV infection amongst haemophilia B sufferers is lower and I believe reflects:-

(a) the temporal, geographic and demographic aspects of the spread of AIDS which appeared in the United States before spreading to the United Kingdom and Europe:

(b) the fact that Factor IX was manufactured exclusively from plasma which was voluntarily donated in the U.K. generally by categories of person who were less likely to be carriers of the virus than the paid donors who provided plasma used for the production of commercial Factor VIII.

82. By the 1st December 1982 when CBLA took over responsibility for BPL, arrangements were well in hand to ensure an adequate supply of FFP from Transfusion Centres to match the manufacturing capacity. From 1982 until the commissioning of the new manufacturing facility by 1988 the supply of FFP from Blood Transfusion Centres to BPL/PFL and the capacity to fractionate, were broadly in balance. I would add that the CBLA had no control over Regional Transfusion Centres and were not responsible for providing the finance necessary to facilitate any increase in plasma supply.

SELF-SUFFICIENCY IN DETAIL

Background prior to the establishment of the CBLA

83. In about 1974/75, approximately £400,000 was spent on enlarging the Scottish fractionation capacity at PFC Liberton. Mr. John Watt, Director of the PFC who was involved in planning the extension to the PFC, specified a final fractionation plant which had the capacity to fractionate 6,000 litres of FFP per week which was in excess of that officially defined. Against insufficient budget provision, the capacity of the manufacturing plant was maintained at the expense of other essential elements e.g. warehousing and final processing. He proceeded with the extension of the fractionation plant at this capacity although the ancillary equipment and buildings could not support its effective utilisation in full. It is believed the view was held that further funds were available should

the plant be required to be extended to its full potential capacity at a future date.

Background prior to 1982

84. In 1977, so far as England and Wales were concerned, there was not yet enough FFP being provided to keep BPL at Elstree working to capacity.

85. As early as 1977, attention was focused on the potential of PFC Liberton to fractionate plasma collected in England and Wales. At a meeting of Haemophilia Centre Directors on 13th January 1988 (minutes - document no 486), Dr. McDonald from the Royal Infirmary, Glasgow, said that Liberton had the capacity to make 60m. iu Factor VIII per year. He added that to reach this target the Centre would need about £25,000 for new capital equipment and money for extra running costs including payment for staff operating a 24 hour shift system. [This figure was nonsense, but was not apparently challenged in the meeting if the minutes are correct.] As I shall describe below, it subsequently became apparent that Scotland was not in a position to make any real contribution to the requirements in England and Wales for Factor VIII concentrate, but at this meeting a comment was made that it seemed as if Liberton had capacity to supply Factor VIII for the whole of the United Kingdom. In fact Dr. Waiter said, at page 12, that the DOH together with the Scottish Home and Health Department ("SHHD") were planning the supply of Factor VIII on a UK basis:

> "Plans had been made to divert plasma from south of the Border to Liberton when Mr. Watt was ready to receive it. It was planned that the Factor VIII made from this plasma would return to Centres south of

> the Border. Agreement in principle had already been reached between the DHSS in London and the SHHD."

In fact, so far as I can tell, whatever plans the DOH may have had, nothing ever came of them.

86. During March 1977, it is clear from the correspondence that there was an exchange of products between Oxford and Edinburgh with a view to Edinburgh conducting some quality comparisons on batches of Factors VIII and IX.

87. It has been agreed that Edinburgh would receive up to 25 tonnes of English out-dated plasma for fractionation on an annual basis. An experimental fractionation to stable plasma protein solution ("SPPS") showed significant differences between specifications of Scottish SPPS and BPL plasma protein fraction ("PPF") - 4.5% human albumin solution. No further fractionation of BPL outdated plasma was entertained.

88. In September 1977, Dr. McDonald of the Royal Infirmary Glasgow wrote to Dr. Maycock (document no. 577) as follows:-

> "With reference to our previous discussion and correspondence, you will recall I was invited by the National Haemophilia Directors to arrange a meeting between representatives of the Scottish Home and Health Department, the DHSS, Haemophilia Reference Centre Directors and those concerned with fractionation, to discuss the problem of the availability of plasma, fractionation, and the availability of Factor VIII products.

From the replies I have received, it would appear there is no great enthusiasm for such a meeting and therefore I have no alternative but to indicate to you that this meeting will now no longer take place."

89. At a meeting of the Scientific and Technical Committee on 26th September 1979, Mr. Harley's position paper STC(79)7 (document no. 934(d)) was tabled. Under the heading "Other Considerations", there is reference in paragraph 13(a) to investigations which were then underway to determine whether the PFC in Edinburgh should be utilised to assist in the fractionation of English plasma.

90. Dr. Dunnill, who was very much an advocate for the Scottish PFC (and indeed had been involved in the development of the equipment installed at PFC which was intended to provide for continuous production), raised, at page 4 of the minutes, the question of the absence of PFC representatives on the Scientific and Technical Committee. I remained concerned about the claims made of PFC by Mr. Watt. Mr. Smart suggested that to clear the path for a decision to redevelop BPL, the claims for PFC be tested. Mr Watt and Mr Cash for PFC were required to agree to a trial of fractionation. I deal with this in more detail below.

91. On the 18th June 1980 I was present at an ad hoc meeting of the Regional Transfusion Directors (document no 1048) at which it was noted that the Director of the PFC Liberton had indicated that he was in a position to fractionate any plasma that the Birmingham Regional Transfusion Centre might care to send to him. The Regional Transfusion Directors agreed that the aim should be to see that PFC was in a position to fractionate all the Birmingham Regional Transfusion Centre's and for that matter other regions' plasma. Mr. Dutton of DOH undertook to speak to the SHHD to ensure that any offer from PFC was made formally through the correct channels between Departments.

92. On 4th July 1980, Dr. Dunnill wrote to the Health Minister, Dr Gerard Vaughan, reporting on the deliberations of the Protein Fractionation Technology Working Party (document no 1063). Dr. Dunnill ~~makes~~ made a case for closer collaboration between England and Scotland. [Throughout this period I was unconvinced that Scotland had the ability to assist England to any great extent despite what I regarded as excessive claims made from time to time by Mr. Watt.] Dr. Dunnill, as I have mentioned, was involved in developing some of the equipment used at PFC Liberton and therefore sympathetic to the continued Scottish involvement and participation through PFC. As his letter makes clear, he was sensitive to the fact that this was certainly not an opinion I shared.

93. On the 18th July 1980, Dr. Dunnill wrote to me (document no. 1068) enclosing a copy of his letter to the Minister. In the second paragraph of his letter, he pursues his wish for closer links between England and Scotland. He knew that proposing the participation of Mr. Watt in the Protein Fractionation Technology Working Party was likely to cause some difficulties as far as I was concerned (and, for that matter, some others,) but his perseverance eventually resulted in Mr. Watt joining the Working Party.

94. In 1981 it remained to be shown whether PFC Liberton had sufficient capacity and adopted working conditions to share the fractionation capacity of the United Kingdom with BPL. A trial of 24 hour continuous fractionation was run towards the end of 1981 at PFC Liberton which ultimately proved unsuccessful and lead to the expressed view by SHHD that the redevelopment plans for BPL should not take Scottish requirements into consideration.

95. The future role of PFC Liberton was raised by Mr. Meakins of the School of Pharmacy and Pharmacology at the University of Bath who wrote to the Times

on the 2nd January 1981 (document no. 1159). This followed a course at the University of Bath at which Mr. Watt had made a presentation setting out his view on PFC's potential. Mr. Meakins suggested that the insufficiency of blood products in the United Kingdom was "largely self imposed by bureaucracy" and went on to say:-

> "Blood processing is carried out for the National Blood Transfusion Service (of England and Wales) at the Elstree plant, whilst the Scottish National Blood Transfusion Service has its own Laboratory in Edinburgh. The output from Elstree is limited by the plant and process which are largely outmoded and inefficient by modern standards. In contrast production in Scotland is limited by the blood supply; the plant at Edinburgh is seriously under utilised, working at less than one third of its current capacity. On more than one occasion a Director of a Regional Transfusion unit, south of the border, has stated that blood collection could be doubled if only Elstree could process it. Because the Health Departments for England and Wales and Scotland are independent, blood is not sent north across the border.
>
> "In my view this state of affairs is nothing less than scandalous in the current deficiency situation which is disadvantageous to both patients and the tax payer."

96. This was incorrect. PFC Liberton's equipment was designed for continuous operation and one stage in a multi-stage process had a potential capacity of an estimated 6,000 litres per week. This capacity as was shown in the above mentioned trial, was not matched by similar capacity in other stages which both preceded and followed: likewise the stage in question required 24 hour manning - a situation never agreed or accepted by the work-force. When, during

the course of 1981, there was a detailed comparison of the BPL and PFC products, my impression, [to the extent that we could get to the truth of the matter,] was that the PFC products were of a lower specification. The trial which subsequently took place clearly showed that without substantial investment in building new facilities and installing additional plant and equipment up and down stream of the central processing plant and equipment, PFC Liberton could not operate to the stated capacity.

97. I should mention that Dr. Meakins' letter also misrepresents the position with regard to plasma supply at the time. During the period 1981-1985 there was no major imbalance between plasma supply and BPL/PFL's ability to fractionate plasma produced in England and Wales. Obviously any unprogrammed significant increase in plasma supply would have overwhelmed BPL/PFL, but as later events show, the co-ordination of increase in plasma supply and commitment to redevelop BPL both proved difficult to achieve. At the time in question there was no material surplus of plasma which, for want of fractionation capacity, was being wasted and therefore no immediate role for PFC Liberton to play, since they would merely be taking plasma which BPL/PFL needed.

98. Dr. E. Harris replied to Mr. Meakins' letter through the Times (document no. 1166) on 7th January 1981, and pointed out that the question of co-ordinating the facilities at BPL with those of PFC was one which had been receiving urgent attention, and it was clearly something which was in the mind of the DOH at the time,[albeit that I was not privy to their thinking.]

99. On 27th February 1981, Dr. Dunnill prepared his Chairman's comments on the Protein Fractionation Technology Working Party report (document no. 1223). In many ways the paper is a summary of the report but there were some [partisan] comments by Dr. Dunnill regarding PFC Liberton on page 1:-

"1. There is uncertainty about the scale of operation required due to the lack of data on UK requirements and uncertainty about the contribution to be made by the Edinburgh Centre. (In the Chairman's view, maximum use must be made of the Scottish facility and the lack of concerted action on this is regrettable).

"2. Multi-shift operation with substantial automation would almost certainly be adopted by an industrial management as a means to reduce capital cost. It would be hampered here by administrative difficulties and by manpower problems in the Elstree region. In this respect, other sites might be preferable, (emphasis added) but removal would cause considerable difficulties in the interim period.

"3. Maximum utilisation of plant could be achieved by continuous thawing of plasma and continuous large-scale fractionation. This option is limited by the lack of experience of truly continuous operation, by the absence of process engineering staff at Elstree, and by the lack of coherent management of Scottish and English facilities. (In the opinion of the Chairman, the immediate institution of coherent management and transfer of staff as appropriate, would be a means to resolve these problems)."

100. In these various comments, one glimpses Dr. Dunnill's sympathies. Whilst automation had been brought into the plant at Liberton (a plant designed in theory for continuous operation), the Laboratory was, nevertheless plagued by manpower problems and the refusal to work shifts. Reference in the third paragraph to "coherent management", was an unrealistic proposition: the real

problems lay in the terms and conditions imposed by the Union, and the structure within the NHS itself.

101. In the Protein Fractionation Technology Working Party's report, the need was identified as a requirement to fractionate some 450,000 litres of plasma a year to meet the projected demand of 90m. iu for Factor VIII per annum. Plasma supply is dealt with in appendix 7 on page 24 and reference is made to the single donation bag, and the fact that the first regional trial of 6,000 single donations of plasma was then under way.

102. The Scientific and Technical Committee met on the 10th June 1981 (see document no. 1304) and amongst other matters, there was reference on page 2 of the minutes to the trials which were being proposed with regard to shift working at PFC Liberton. These trials were planned to take place in October 1981. Their relevance to BPL was stated to be in the context of assessing a target capacity figure for the redeveloped BPL. That is to say, to establish what PFC could contribute and the reduction in the capacity of a redeveloped BPL which could be achieved in consequence.

103. On the 11th June 1981 the DOH circulated paper AC(81)11 (document no. 1307) for discussion at the 3rd meeting of the Advisory Committee on the National Blood Transfusion Service which was due to take place on the 22nd June 1981. AC(81)11 was the preliminary report of the Working Party to Advise on Plasma Supplies for Self-sufficiency in Blood Products dated June 1981. The Working Party noted that, inter alia, an estimated 500,000 kg of plasma were required to meet the requirements for Factor VIII concentrate. It would be possible to obtain 200,000 kg of plasma from whole blood donations and to collect the remaining 300,000 kg of plasma by increasing whole blood collection or by introducing plasmapheresis. The option of plasmapheresis had advantages over

the procurement of plasma entirely from whole blood donations in that the wastage of red cells was avoided, and donor panel size could be reduced because of the increased frequency of attendance of plasmapheresis donors.

104. At the first meeting of the Policy Steering Group (for the redevelopment of the BPL) it was reported (on page 2 of the minutes - document no 1363) that the potential for PFC Liberton to fractionate a proportion of English plasma had not yet been determined. It had been decided not to use a processing system requiring 24 hour shift work in any redeveloped BPL facility. It was recognised on page 3 that spare capacity to process plasma must be built into the BPL in its redeveloped form. As well as an increase in the level of plasma supplied by RHA's, I was hoping for a 20% improvement in yield from FFP over the next two years. It was a general feeling of the Group that the laboratories should be planned so as to meet the target for self-sufficiency whilst at the same time, paying regard to the regions' estimates of likely plasma supplies. The role of the PFC Liberton is mentioned again on page 6, and this reference marks the slight shift in thinking: Dr. Walford suggested that it might prove uneconomical to send plasma to Liberton to fractionate.

105. At the 4th meeting of the Advisory Committee on the National Blood Transfusion Service which took place on the 28th September 1981 (document no. 1387) the question of plasma supply arose. As a result of the most recent meeting of the Haemophilia Centre Directors, it had been decided that target plasma supply required to achieve self-sufficiency could be reduced to 435,000 kg from 500,000 kg based on a presumed process yield greater than 250 iu per kg. The quantity of plasma to be made available in fact changed once heat treatment became a requirement because earlier yield assumptions were invalidated. On page 3, it is clear that Mr. Harley of the DOH again hinted that PFC Liberton might be jointly meeting the UK's needs for blood products with any redeveloped

BPL. "Further discussions" would be needed between the DOH and the Scottish Home and Health Department.

106. Another matter for discussion was the future role of the Working Party on Plasma Supplies for Self-Sufficiency in Blood Products. Its important role in terms of increasing plasma supplies was recognised. However, it was noted that the Working Party was merely an advisory body with no executive powers.

GAP

107. On the 2nd October 1981, Mr. Godfrey of the DOH prepared an action list (document no. 1391) following the meeting of the Policy Steering Group referred to above. Mr. Smart was the Chairman of the Policy Steering Group. I discussed the problems associated with PFC Liberton and the claims made for it with him, and he had suggested that we should again try to resolve the extent of PFC's role by a trial of fractionation. [Given the claims for PFC capacity it is surprising that the proposed trial was not actively undertaken and that so much delay in implementation actually occurred]. As a prelude to any further review, both BPL and PFC were to provide product specifications.

108. In a letter by Mr. Watt to the Scottish Home and Health Department dated 14th October 1981 (document no. 1397), he set out certain data in relation to PFC Liberton products which was part of the exercise instituted by the DOH to ascertain the role which PFC Liberton might be able to play in the provision of blood products. PFC Liberton did not in the course of time produce all the relevant data. In particular under the heading "Factor VIII Concentrate", Mr. Watt states that the specifications of the product being issued from PFC were in a state of change.

109. With regard to what is said on the second page of the letter under the heading "Stable Plasma Protein Solution" [I should perhaps clear up one point which arises from Mr. Watt's misdescription of the English albumin product. He

deliberately obscures the true nature of the albumin products produced in England and in Scotland.] He refers to "English SPPS" but in fact BPL produced Plasma Protein Fraction ("PPF") which is a purer product than SPPS by pharmacopoeial definitions.

110. [I mention this not because of its particular relevance to HIV, but simply as an illustration of the general misinformation which was spread around to promote the cause of PFC at various times. This carried through into the product specifications themselves which appear immediately behind the letter.]

111. On the 19th October 1981, the Policy Steering Committee met again and the action list arising from that meeting (document no. 1405) records the arrangements to witness the trial production run at PFC Liberton. It can also be seen from the minutes that in the context of the discussion about the proposed trial of PFC Liberton, they had not been receptive to the idea that we send observers (an idea which originated with me).

112. Mr. Godfrey of the DOH sent under cover of his letter of the 2nd November 1981 (document no. 1416) what I believe was the final form of documentation setting out the product data from both BPL and PFC which was to be used for comparative purposes in conjunction with the trial at PFC Liberton. In his note of 5th November 1981 (document no. 1417) Mr. Vallet deals with the matter that I have mentioned above, [i.e. the deliberate misdescription of the UK albumin produced, and points out that the misuse of the nomenclature is somewhat surprising, given that Mr. Watt had for many years been on the Blood Products Panel of the Pharmacopoeia Europa.]

113. On the 24th November 1981 there was a meeting of the Scientific and Technical Committee and amongst the various matters discussed, the minutes

(document no. 1436) record that the shift working experiment had been carried out at PFC Liberton, (although the report on the exercise was not available until January 1982). The plasma used was BPL outdated plasma supplied to PFC some time previously. The PFC trial related only to an evaluation of continuous production of SPPS: Factor VIII production was not included and therefore outdated plasma could be used. Mr. Wesley, head of the Large Fractionation Department at Elstree, supervised the PFC shift work experiment. Dr. Dunnill felt that certain benefits would be derived from the shift work exercise:-

"1. An indication as to whether PFC could handle more plasma;

2. The advantages or disadvantages of a continuous operation system."

114. The PFC trial was considered at the meeting of the Policy Steering Group that took place on the 18th December 1981 (document no. 1447). Paragraphs 6, 7 and 8 deal with the trial. Mr. S. Hibbert reported that PFC was capable of improvement, although adjustments would have to be made to its layout if the (then) system of production were changed to facilitate continuous production on a shift work basis. He commented that, as constituted, PFC appeared less cost effective than BPL, but also that PFC hoped it would eventually service the northern English Region. Mr. Hibert said that he did not expect the findings of the exercise to prove conclusively that continuous working would overcome the shortcomings of the existing system, but the experiment had shown that the equipment could function on such a basis. I expressed reservations regarding the experiment in that the study had concentrated on one stage only of what was a complete production process. It was all very well fractionating plasma on a continuous basis, but the facilities both up and down stream had also to be capable of handling the raw product and end product from the continuous manufacturing process. The experiment at PFC Liberton was inconclusive (as

paragraph 7 of the minutes show), and the commitment of the SHHD to PFC Liberton would be critical to the mode of its future use.

115. Mr. D. Wesley's report on the PFC Liberton trial became available around the turn of the year, and on the 5th January 1982, I sent David Smart a copy, (document no. 1458). It seemed to me that the report supported my concerns about PFC Liberton's ability to assist England and Wales in the production of Factor VIII, since the trial was unrepresentative of what would happen in practice. The product produced on a continuous basis during the experiment was SPPS prepared from time-expired plasma and not Factor VIII or other blood products prepared from FFP. By concentrating production on this one product, the experiment gave at best a distorted picture of PFC's ability. My own feeling was that the experiment was inconclusive. In his report, David Wesley noted that:-

- the CSVM (continuous small volume mixing) system which lay at the heart of the PFC fractionation plant, was capable of continuous operation for periods of at least 120 hours, and that there was no reason to believe that the system would not be operated permanently for such periods with 48 hour breaks at weekends for maintenance, etc.;

- there was no data to indicate how purity of yield of the product was affected by truly continuous CSVM fractionation;

- with the available bulk fractionation equipment, continuous fractionation would prevent the production of immunoglobulins and salt-poor albumin;

- during the feasibility exercise, Factor VIII production was limited to the normal quantity. No evidence was available from the exercise to

suggest what increase could be made to such production by the fractionation of a large volume of FFP;

- with the exception of quarantine storage through to inspection and despatch, all support sections appeared to have capacity to handle the product from 1,000 litres of time expired plasma per day;

- storage space throughout PFC was at a premium and increased production would probably place an even greater strain on an already overloaded system.

116. David Wesley's report was also useful in that it contained a description of the continuous fractionation process which PFC Liberton employed and which they called CSVM. As can be seen from the report, it was necessary if continuous operation were to be introduced, to reach a special agreement with the Trade Unions to work on a shift basis. There were considerable reservations expressed at the time and later as to whether or not the Trade Unions would indeed be prepared to work on a shift basis or at least one which made economic sense. On the 5th January 1982, I also sent a copy of the report to Mr. Godfrey at the DOH.

117. There followed a very important letter written by the SHHD to the DOH dated the 11th January 1982 (document no. 1462) which, concluded that PFC would not be considered in the future planning of self-sufficiency in England and Wales.

[QUERY: IS IT SUFFICIENT TO RELY UPON THIS LETTER AND TO DISPENSE WITH THE EARLY HISTORY OF DISCUSSIONS RE THE USE OF PFC?]

118. The letter begins with the suggestion that PFC could make a substantial contribution towards processing English plasma, but this positive statement then becomes submerged beneath a series of very serious caveats which collectively qualify the letter to such an extent that subsequently no further consideration was given to PFC Liberton assisting in the fractionation of English and Welsh plasma. The letter repays reading in full, but the essential qualifications were:-

(a) the need to negotiate terms with the relevant Trade Unions through the Whitley Council machinery to operate on a shift work basis (something which would almost certainly have had quite substantial cost implications);

(b) the need to invest some £6m. to £7m. to expand ancillary facilities to cope with the workload, e.g. in relation to the provision of space for freeze-drying, packaging, labelling, storage, etc. This estimate itself could scarcely be relied upon, since Mr. McPherson, the author of the letter, made it clear that it was not possible to give any detailed breakdown of this "estimate";

(c) it was suggested that the work (for which no estimate was available) could be completed in 2½ years, but again the general uncertainty which pervades the letter, gives the impression that this too could not necessarily be relied upon;

(d) particularly significant, however, is a statement in the letter that the revenue implications of fractionating plasma at Liberton to produce, inter alia, Factor VIII had not been costed. In short, no clear idea of the cost of using PFC Liberton could be given.

119. In summary, it was clear that without substantial changes in working practices, an investment of some £6m. to £7m. (but with no guarantee this was an accurate estimate), a delay of some 2½ years (again with no guarantee that this was an accurate estimate), PFC Liberton would be in a position to fractionate sufficient amounts of English plasma but at a cost which no one could predict.

120. At paragraph 6 of the minutes of the meeting of the Policy Steering Group held on 1st March 1982 (document no 1485), there is a record of Mr. Harley's report to the meeting on the letter received from SHHD following the PFC Liberton "experiment". He said that PFC Liberton would not be able to fractionate any substantial quantity of English plasma without the introduction of a three shift working system. Mr. Harley had asked the DOH personnel division to consult with the Scots on the possibility of reaching an agreement on such a system, but was not hopeful of obtaining even a preliminary answer before the end of April. The Group agreed with SHHD that in these circumstances the redevelopment of BPL should not be planned on the basis that there should be any anticipated contribution from Liberton. Mr. Harley was asked to seek approval from the JMC to proceed on the assumption that for planning purposes, BPL would process all plasma for England and Wales. The estimated production capacity of the new laboratory could be revised if necessary at a later date, if there were a substantial change in Liberton's position. In the event, bearing in mind the other points made in the SHHD letter, I do not think that the shift working system was the sole obstacle to increasing capacity. This is borne out by a paper which the DOH personnel later produced for the Minister (to which I contributed) on which I comment below. Clearly there was time and a great deal of money involved in any up-grading of Liberton, and a good deal of uncertainty as to the economic wisdom of this course of action.

121. On the 31st March 1982, the Advisory Committee on the National Blood Transfusion Service met and, as will be seen from the minutes (see document no 1495), there was a discussion of the progress in formulating arrangements for fractionating plasma from Northern Ireland at PFC Liberton. The logistics of transport were in the process of being ironed out, and it was hoped to begin operations by the end of April 1982 (operations subsequently began and at the 6th meeting of the Advisory Committee held on the 15th September, it was reported that batches of plasma from Northern Ireland had been satisfactorily processed at PFC Liberton) (see document no. 1551). There was an endorsement of the figure of 435,000 kg of plasma per annum as the amount necessary to achieve self-sufficiency in blood products in England and Wales. I confirmed (see paragraph 8) that the up-graded BPL now had capacity to process all available FFP.

122. On the 18th May 1982, Mr. Godfrey of the DOH wrote to all members of the Advisory Committee on the National Blood Transfusion Service, and enclosed a summary of our production during the financial year 1981/82. He also enclosed a Parliamentary Question announcing the establishment of a Special Health Authority to manage the Central Blood Laboratories (see document nos. 1511, 1511(a), 1511(b)). Confirmation of the decision is also to be found at paragraph 9 of the minutes of the 13th meeting of the Scientific and Technical Committee (document no. 1521) held on the 21st June at which Mr. Harley of the DOH reported that Ministers had agreed to the establishment of the Special Health Authority and were being consulted on the Authority's name and constitution. It also records that Mr. Smart had accepted the invitation to be the Authority's first Chairman and that it was hoped that the new Authority would come into being on the 1st November 1982 - in the event it was the 1st December 1982.

123. At the end of July 1982, a memorandum which I had prepared in conjunction with Mr. Angilley from the DOH was completed (see document no.

1536). I contributed quite considerably to this paper, which was to contain a financial appraisal of the various options for the redevelopment of the BPL for submission to the Treasury. It should be noted that in paragraph 3 the memorandum repeats the reasons why PFC Liberton was eventually dismissed as a possible contributor to the fractionation of English and Welsh plasma. The conclusion (see paragraph 28) was the recommendation to build a 400 tonne laboratory at a cost which was then budgeted at £21.1m. spread over the years 1982/3 to 1985/6. The uncertainty with regard to plasma supply was reviewed in paragraph 30, together with the need to ensure that, at the same time as BPL was being redeveloped, there was an increase in the supply of raw material for fractionation.

124. On the 11th November 1982 a press release was made by the DOH (document no. 1568) announcing the formation of the Central Blood Laboratories Authority and the release also gives information regarding the membership of the Authority which, as I have indicated above, was to be chaired by Mr. D. Smart.

125. The first meeting of the CBLA (albeit an informal meeting) took place on 3rd December 1982 (see minutes - document no. 1574) but the meeting was preceded by a letter from the Minister (Norman Fowler) to Mr. D. Smart dated the 17th November (document no. 1569) in which the Minister set out his views on the functions to be performed by the CBLA. In this regard, the annex to the letter is also relevant in that it sets out the main tasks of BPL and PFL. A letter written on the 30th November by Mr. Illingworth of the DOH to the Secretary of the CBLA (document no. 1570) enclosed directions by the Secretary of State for the CBLA setting out the requirements for exercising the building and engineering functions of the Authority. The delegated limit for building and engineering works was £150,000.

126. However, in the papers for the CBLA meeting on the 3rd December 1982 which were attached to the agenda (document no. 1573) it was made clear in relation to the agenda item dealing with the redevelopment of BPL, that after consideration of an investment appraisal prepared by DOH with the assistance of the former JMC's Policy Steering Group, and following advice on the supply of plasma from the Advisory Committee on the National Blood Transfusion Service, DOH Ministers and the Treasury had agreed that BPL should be redeveloped at a size:-

(a) capable of making England and Wales self-sufficient in blood products (i.e. an annual through put of 400,000 kg of fresh frozen plasma), and

(b) capable of extracting all therapeutic products from the plasma, those products surplus to NHS requirements to be sold to the pharmaceutical industry.

1983

127. Supplies of FFP at this time were gradually increasing. Although there was a suggestion that supplies of FFP were reaching a level where BPL no longer had the capacity to fractionate all the FFP which was available, this was not correct. My letter of 17th January 1983 (document no. 1594) addressed to Dr. Wagstaff who was the Director of the Regional Transfusion Centre at Sheffield, followed up on criticism which was levelled at BPL at the 187th Regional Transfusion Directors' meeting which took place on the 14th January 1983 (document no. 1593). In particular I dealt with the suggestion that plasma supplies were being improved through the introduction of optimal additive solutions ("SAG M"). Red blood cells re-suspended in SAG M form a product

suitable for clinical use having an extended shelf life of up to 35 days. It was alleged that this increase in plasma supply was not being matched by increased product from BPL - this was not the case and I felt it necessary to put the record straight.

128. The document which is attached to my letter is an extract from the Blood Preservation Working Party documentation which was discussed at the meeting on the 14th January 1983 and contained several suggestions which were not true. (The constitution of the Blood Preservation Working Party is described in Appendix 2; it was a Sub-Committee of the Regional Transfusion Directors' meeting, concerned primarily with the production of frozen blood). A single plasma pack had been introduced and we had found the change was accepted only with some reluctance by certain Regional Transfusion Centres. It became necessary to design a larger bag to take the extra volume of plasma resulting from the introduction of the use of SAG.M. This anticoagulant additive allowed Transfusion Centres to increase recovered plasma volume per donation from approximately 200 ml to approximately 280 ml. As far as yield was concerned, the comments in the note were simply wrong. Together with others, I had spent a great deal of time explaining the logic and purpose of a single donation pack, and yet here was a Working Party advocating continued use of the 5 litre pack. On top of all this, some of the members of the Working Party were in favour of SAG.M whilst others were not. I replied that the Working Party's criticisms of BPL were unfounded. I circulated figures at the meeting on the 14th January 1983 which confirmed that BPL had in fact managed to make a substantial increase in Factor VIII productivity. I supported the SAG.M programme and confirmed that a major research commitment towards improved Factor VIII yields existed at BPL.

129. I continued to do what I could to encourage increases in FFP production in anticipation of the new BPL facility. On 25th May 1983, I prepared a document entitled "Budget - Function Relationships - Blood Products Laboratory, PESC Estimates related to BPL Manufacturing Requirements", (document no. 1638). This document was developed for a talk which was given to the Transfusion Service at a Travenol annual symposium. The paper and its supporting documentation was intended to show the future demands for plasma to service the new BPL plant which, at the time, we anticipated would be commissioned in December 1985, and would have a capacity to fractionate 450 tonnes of FFP per annum.

130. At a meeting of the Advisory Committee on the National Blood Transfusion Service on 17th October 1983 (minutes - document no 1689), there was discussion (see particularly paragraphs 16 to 19 of the minutes) of the need to dramatically increase the supply of FFP if self-sufficiency were to be achieved. I explained at the meeting that we had mounted a campaign to make the Regional Health Authorities fully aware of BPL and the long term benefits to the Authorities of increased plasma procurement, in line with the findings of the earlier investment appraisal: DOH representatives said that they would discuss with the CBLA what assistance might be given by the DOH in reaching RTO's (Regional Teams of Officers). In fact this assistance was never forthcoming. Interestingly, it will be seen that supplies of FFP to BPL in the first six months of 1983 amounted to 73,704 kg showing that, on an annualised basis, FFP supplies were showing a reasonable increase over the previous year where the total had been 127,000 kg.

131. I produced two documents during the course of 1983 which were designed to try and increase awareness of the need to improve the supply of FFP.

132. The first of these was a paper I prepared entitled "Plasma Supply-National Blood Transfusion Service" (document no. 1704) which is designated RTD(83)(7) (which was discussed at the 188th RTD meeting on 18 May 1983-minutes document no. 1637). The paper was intended to bring together a number of threads (the information regarding BPL's development, likely future capacity and requirements for plasma) to inform Regional Transfusion Centre Directors what was required for the future. As can be seen from page 10 of the paper, the development of national projections was the subject of a further document prepared by Mr. N. Pettet which drew to the attention of Regional Transfusion Directors the idea of a five year plan aimed at supplying the projected plasma needs of BPL. I would draw attention particularly to fig.3 which shows what was required in terms of FFP to supply a maximum input of 440 tonnes using a mixture of recovered plasma, SAG.M plasma, and plasmapheresis.

133. The other document prepared in 1983 for the Travenol symposium for the National Blood Transfusion Service dealt with the value of SAG.M systems in the provision of plasma products (document no 1705). Again, the idea was to inform the Transfusion Service of the advantages of using SAG.M which, if accepted by clinicians, would have a major impact on the plasma procured by NBTS for supply to BPL.

1984

134. The 10th meeting of the CBLA took place on 25th January 1984 (document no. 1722). Mr. Watt was no longer the Director of PFC Liberton. The Scottish Blood Transfusion Service had reported to Mr. Smart that a recurring surplus of Factor VIII was forecast and that their surplus stocks could be made available to BPL for distribution in England and Wales. In fact Scotland made

available one lot of Factor VIII comprising some 2m. iu, which we subsequently distributed.

135. On the 8th March, Dr. Kernoff sent me a copy of a draft of a paper he was to present at the Haemophilia Society Residential Seminar on the 10th March (document no. 1737). The paper, entitled "Blood Products and their Problems" touches upon a number of areas of concern: heavy reliance in the NHS on imported commercial blood products; the inability of the Transfusion Service to meet the plasma requirements of the country; lack of co-ordination between the policy makers and those implementing the policy at Regional Blood Transfusion Service level; the emphasis placed on the collection of whole blood, rather than its separate components.

136. At the 11th meeting of the CBLA which took place on the 28th March 1984 (document no. 1756), Dr. Harris' comments at the bottom of page 2 in relation to plasma supply are characteristic of the shambles which existed at that time.

137. At the 9th meeting of the Advisory Committee on the National Blood Transfusion Service which was held on the 10th April 1984 (minutes - document no 1761), it was noted that, due to resource constraints within Regions, Regional Transfusion Directors were less optimistic of attaining their targets towards increasing the supply of plasma to BPL to a self-sufficiency level, than they were in mid-1983. To an extent, this and the work which followed demonstrated that it was no small feat to increase the supply of FFP to the level where there was sufficient to service the new facility at BPL.

138. The possibility of a contribution of Factor VIII by the Scottish National Blood Transfusion Service was again touched upon in a letter from Mr. Perry to

Mr. Pettet of BPL on the 8th June 1984 (document no. 1776). The first proposal on the part of the Scots was to supply a total of between 7m. and 9m. iu to BPL for distribution in England and Wales. It was stressed that a "regular supply commitment" could not be made.

139. However, Mr. Perry's letter (he was the acting Director of the PFC in Edinburgh at the time) of 7th September 1984 (document no. 1808) confirmed that only 2,123,500 iu of Factor VIII concentrate would be delivered to BPL (on Friday, 14th September). This amounted to 8,320 vials each with an average content of 230 iu per vial. He commented at the end of his letter that we should not plan on any additional quantities being available.

140. My circular letter to Regional Transfusion Directors of the 3rd August 1984 (document no. 1795) deals, inter alia, with arrangements for an "up-date" meeting to be held at BPL on the 18th September 1984. As the timetable and agenda make clear (document no. 1816), the plan was to show those attending around the new factory which was of course in the process of construction, and to discuss various matters of common interest but, of particular relevance to the present litigation, plasma procurement and supply, plasmapheresis trials (then underway) and the supply of Scottish Factor VIII. In addition, the BPL development was a general topic of discussion. Again, this evidences the dialogue which we sought to promote at various times with the Regional Transfusion Directors. The Scottish Factor VIII was to be made available in September/ October and was to form an addition to the normal pro rata allocation to Regional Transfusion Centres.

141. The CBLA met again on the 26th September 1984 (document no. 1822) and the redevelopment work was proceeding at that point to the extent that there were concerns regarding the levelling off (or so it seemed at the time) of the

supply of FFP. [TO EXPAND: DID CBLA PROPOSE DOING ANYTHING ABOUT THIS?] It is interesting to note Dr. Gunson's comment (paragraph 69.2) that the requirement for Factor VIII was, by that time, in excess of 100m. iu per year.

142. In October 1984, Mr. Perry wrote to BPL (document no. 1826) indicating that he had some 2,000 vials of Factor VIII (460,000 iu) at PFC which had failed to meet their defined finished product specification. He said that, bearing in mind the tentative evidence that was emerging in relation to the infectivity (AIDS) status of commercial product, Haemophilia Directors in England and Wales might consider that the use of this "sub-specification" product was preferable to the use of commercial concentrate, and he enquired whether BPL would be interested in taking a supply. In the event, I wrote on the 1st November 1984 (document no. 1838) confirming that just as we would not wish to send out batches of our own product which failed our quality control test, we would really have to take the same line in relation to Scottish product.

1985

143. Plasma supply was considered during the course of the meeting of the CBLA which took place on the 1st February 1985 (document no. 1932). By this stage, Dr. Harris, the Deputy Chief Medical Officer, was no longer a member of the CBLA. There is reference in the minutes at paragraph 5/85 to the position with regard to plasma supply, and the fact that heat treatment would reduce the Factor VIII yield with the consequential requirement to ensure that plasma supply was adjusted accordingly. Dr. Gunson was encouraging the use of plasmapheresis, and, as the minutes make clear, for the appropriate level of central funding for its more widespread application. Of course plasmapheresis had by this time become well established as a procedure and sufficient funding was of primary importance.

144. By 1985, the issue of self-sufficiency was receding. As will be seen from a letter which I wrote to Dr. Collins of the Regional Transfusion Centre in Newcastle on the 12th April 1985 (document no. 2048), (acknowledging receipt of the agenda for the forthcoming meeting of the Regional Transfusion Directors to be held on the 17th April 1985), I commented on the absence, both in this agenda and its predecessor in 1985, of any reference to the questions of plasma supply and self-sufficiency.

145. In the event, plasma supply was discussed at the 18th meeting of the CBLA held on the 22nd May 1985 (document no. 2093). Dr. Gunson reported that a meeting had been held to consider data received by the DOH from Regional Transfusion Centres on projected volumes of plasma to be supplied over the next four years. The meeting noted there was a principal shortfall from four Regions. **[The minutes of the relevant meeting are said to be attached as an appendix but they are not].**

146. In November 1985 at the 11th meeting of the Advisory Committee on the National Blood Transfusion Service held on the 6th November (document no. 2202), I again reported on progress on the BPL redevelopment project and stated that commissioning would be gradual. I expressed concern about maintaining a quarantine supply of plasma. Mr. Williams of the DOH advised the meeting that the plasma supply situation seemed to be improving with the forecast being a supply of 400 tonnes against 435 tonnes demand. It was agreed at the meeting that the DOH would continue to monitor the conversion of Regions' firm promises into action plans for plasma production. At this stage, therefore, it can be seen that the DOH were playing a rather more direct role than historically had been the case in encouraging increases in supply to keep BPL functioning.

1986 AND BEYOND

[TO DO]

SUMMARY OF SELF-SUFFICIENCY CLAIMS AND CBLA REBUTTAL

147. Turning to the particulars of negligence and/or breach of statutory duty by the CBLA in relation to the issue of self-sufficiency in the Blood Transfusion Service, it may be helpful to summarise the points which emerge from what I have said above, and relate these to the particular claims raised against the CBLA.

148. (95(g)) Failed, from 1982 or such later time as may be justified on the evidence of trial, to advise the Department of Health and the Health Authorities to use the spare production capacity in Scotland to eliminate or reduce the Welsh and English need to import commercial Factor VIII concentrate

[THIS MAY BE AMENDED TO INCLUDE CBLA'S FAILURE TO SUB-CONTRACT THE FRACTIONATION OF PLASMA COLLECTED IN ENGLAND AND WALES TO SCOTLAND]

This issue had been run to ground shortly before CBLA took over BPL. From the period I first joined BPL up to 1982, BPL had been haunted by the spectre of PFC Liberton and the [grandiose] claims made for it by those responsible for its administration (who were hardly independent). I think it is clear from the material to which I have referred above, that the trial carried out at PFC Liberton with the intention of determining what its spare capacity might amount to was, at best, inconclusive and it resulted in the SHHD making it clear to the DOH that PFC Liberton was not in a position to assist without substantial expansion of its facilities which would take a considerable period of time to achieve, a considerable amount of money and, moreover, require a radical alteration to existing working practices. By the time CBLA took over, the die

was cast and the DOH were determined that BPL should be redeveloped on a scale which would achieve self-sufficiency without any contribution from Scotland. The assistance which Scotland was able to provide came in the form of a "once and for all" contribution of some 2m. iu of Scottish Factor VIII which was promptly distributed to Regional Transfusion Centres. Despite suggestions that more might be available, it was not forthcoming. The belief that there was any significant spare capacity immediately available for fractionating English and Welsh plasma at PFC Liberton was, I believe, a myth. However, quite apart from this, there was no major imbalance at any time between 1982 and 1985 (after which the issue became irrelevant) between the supply of FFP from English and Welsh Regional Transfusion Centres and our requirement to fractionate it.

149. (95(h)) Failed, from 1982 or such later time as may be justified on the evidence of trial, to advise the Department of Health and the Health Authorities to use plasmapheresis to boost the yield of plasma from volunteer donors in England and Wales so as to eliminate or reduce the need to import commercial Factor VIII concentrate

Again, I think that the facts as outlined above show that we took all reasonable opportunities to advise both the DOH and the Health Authorities as to how FFP production might be maximised. This included the increased use of plasmapheresis, but this required additional investment and we were in no position to provide the funding or to force the DOH or the Regional Health Authorities to do so. The advice to all concerned with regard to boosting FFP supplies pre-dates 1982 by some years, but continued after CBLA took over responsibility for BPL.

150. (95(h)A) They failed, from 1982, to approach commercial blood products manufacturers to fractionate plasma from volunteer donors in England and Wales,

and/or they failed to advise the Department of Health and the Health Authorities to do this

Again this allegation assumes an excess of FFP which BPL/PFL were unable to fractionate. Of course had RHA's and the DOH injected substantial funding into the NBTS, there was a possibility that the FFP supply might have outstripped our capacity to fractionate it, but this was not the case at least from December 1982 to December 1985.