File 28

JMC CL (82) 16

- replaces JMC CL (82) 12

ANNUAL REPORT 1981/2

Blood Products Laboratory,
Elstree, Herts.

Plasma Fractionation Laboratory,
Oxford.

R.S. LANE, MD MRCP MRCPath,
Director.

20th April 1982.

1500

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Input of frozen fresh human plasma to BPL increased for the first time in five years; it was all fractionated to Factor VIII with only minimal losses and output of intermediate VIII concentrate and other main products increased accordingly. Concomitant with this improved production was the major disruption of the interim building refurbishment.

The laboratory and staff progressively accommodated the philosophy and practical implications of Good Manufacturing Practice and other regulatory requirements. The major design faults of BPL remain, however, and continue to exert a real compromising effect on laboratory performance and product safety. The need to define an early target date for completion of a new BPL process factory cannot be understated. BPL is now approaching capacity or above capacity in all mainstream activities from raw material supply and fractionation to quality control and research and development. Perhaps the two most oppressive shortcomings are the inability to bring on-line new products for clinical use and the lack of capacity permitting full economic fractionation of the existing resource. Thus the interim refurbishment of BPL only allows for improved product safety and production volume to a limited degree.

The next two years will see a programme of increased Regional plasma supply aimed at full use of the existing whole-blood plasma resource. This could realise between 150 and 200 tonnes of fresh plasma for fractionation. Management must understand that the greater the success in promoting Regional activities, the greater becomes the risk of stock-in failure of production at BPL.

BPL looks forward to a new permanent management which will provide the terms of reference and operating conditions needed for full economic manufacture of plasma fractions at Elstree.

R. S. LANE,
20th April 1982.

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SUMMARY

1981/82 was a year of achievement through intense, if at times conflicting, activity in the laboratory: there were major production increases despite a heavy programme of building work in the production areas, and consequent GMP problems.

Important increases in released product over 1980-81 were: Factor VIII +39%; Factor IX +38%; and 400 ml PPF +36%. Product released was valued at cost at £7.6 million, of which £4.6 million represents the notional value of the input plasma. The market value of the released material was £12.25 million.

The laboratory has been strongly represented at international congresses and meetings through chairmanship, invitations to speak and in participation in committee work. (Appendices 7a, 7b)

Nine scientific papers were published by staff members, and a further one prepared for publication: (Appendix 6)

Five major research and development projects were progressed during the year, great efforts being put into the chromatographic purification of albumin and preparation of normal human immunoglobulin for intravenous use.

A wide range of collaborative research work has been undertaken, and is listed in the report.

Mr. T. Snape completed his Ph.D. thesis, and was awarded his doctorate.

Total operating costs for the laboratory were contained within the cash limit of £2.897 million. Capital expenditure at Elstree did not fall far short of the cash limit (approximately £1,000 below), despite failure to maintain the original programme of work; however, at Oxford there was a shortfall in capital spending of £18,000. This work will need to be done in the current year.

Notable staff changes were the retirements of Dr. E. Bidwell, Head of PFL, and Dr. G.S. Turner, Head of Virology. The appointments of Mr. G.E. Mallory as Deputy Director (Manufacturing/Administration) and Dr. T.J. Snape as Head of Quality Control will strengthen the manufacturing management at the laboratory. Total staff movements were contained to give a net increase of +6% and a year end total of 184 staff manning both laboratories.

PRODUCTION

Plasma intake: at 116.2 tonnes, the fresh frozen plasma intake was 26% greater than in 1980/81. In the last half year, and particularly in the last quarter, a significant quantity of this was in single donation packs. The intention is to maximise the single pack presentation as soon as possible, to gain both in raw material hygiene and identification, in line with the requirements of Good Manufacturing Practice. This change necessitates mechanical bag opening, plasma crushing and thawing, to gain in productivity and offset the extra manual handling which otherwise would be necessary. Plasma input will therefore become progressively more machine regulated and paced and significant progress in this work will be made in the current year. Time expired plasma intake in 5 litre packs has decreased slightly - 9% less.

The processing of 138.2 tonnes of plasma over the twelve months is significant in the light of the scale of operations possible, and the many interruptions to the production processes especially during the second half of the year. At 138 tonnes the laboratory suffers from diseconomies of small scale working and in many process areas carries the penalties of pilot scale working and/or manual handling. The greater throughputs planned for the near future are welcomed as they will enable the benefits of scale to be experienced in our operations.

Slippage in completion of facilities-upgrading works when units have been released to contractors on time, have caused severe disruption to many areas of production, in particular in Factor VIII and PPF units. In the former this has created a restriction of supply to RTCs which will also continue over the next few months. In the latter, lack of production has caused inroads in stocks of released material. Overall the effects on production of the interruptions have been minimised through the dedication of staff at all levels; their efforts have avoided a serious supply crisis.

From April 1981, the system of distribution of Blood Products has been one of pro-rata returns to the RTCs relative to plasma received from each. This has had the effect of stimulating regions to supply fresh frozen plasma, and in increasing quantities.

A summary of product volumes and plasma input is given in Appendix 1.

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QUALITY CONTROL

The organisation of Quality Control in the Elstree and Oxford laboratories underwent major reorganisation in February 1982, following the appointment of Dr. T.J. Snape as Head of Quality Control. Both units are now integrated as the "Control Laboratory".

A programme of documentation review has begun in both laboratory and production areas and the first round of revision will be completed in the current year. A microcomputer has been purchased and installed in the control unit, for both word and data processing, including documentation and product specification data bases.

The present staff level is 38 with three vacancies to be filled. Dr. G.S. Turner, Head of Virology, retired on 31st December 1981, and there have been no further staff additions.

In July 1981 the routine testing of the antibody content of normal immunoglobulin was taken over by the Virus Laboratory. This had been carried out previously by NIBSC, Hampstead, and at other laboratories.

Radio immune assays for hepatitis B surface antigen have been produced and supplied to all UK Transfusion Centres and some PHLS laboratories, with limited exceptions. Reagents for some 1.5 million tests have been despatched during the year, giving a total income of around £280,000.

35,711 routine tests for hepatitis B surface antigen have been carried out on plasma pools and products, with sixteen positive results. Two of these only were on products pre-release, and are the subject of investigation. The batches used 5L pool material and the sample on the input material tested as clean. It is possible that 5L pool samples are not representative of bag contents. The changeover to single donor packs with individual pack testing at the RTC's will provide greater security against this happening in the future.

European Pharmacopoeia media and test conditions for sterility testing were introduced from 1st March 1982.

Environmental testing has been extended and intensified, and this process will continue in the current year.

With reorganisation continuing, and the ongoing revision of methods and systems, the Quality Control Laboratory will make a significant input this year in our drive to improve practices and standards.

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PRODUCT COSTS

A new set of product costs has been calculated in the detail which the accounting capability allows. These costs take account of the depreciation charge of the capital employed, and include total research and development costs even where the research effort may be unrelated to present day activities. The costs are therefore calculated on the basis of covering all site expenses against the products released.

Input material has been valued at £37.50 per litre of fresh frozen plasma, and £12.50 per litre of time expired plasma. If these are true valuations, then they reflect adversely on blood collection and RTC processing efficiencies and/or are a further reflection of the diseconomies of scale/organisation of these activities.

Plasma valuation is crucial in calculation of Blood Products' costs, as it represents approximately 60% of the final products' cost. It therefore impinges significantly on notional profitability and the notional returns on investments. A list of current product costings, based on the above plasma valuations, is given in Appendix 2. These will be revised as new data becomes available.

Multiplication of unit quantities by unit costs and their summation gives a total product cost valuation of £7.6 million for the year's activity. Similarly the market value of the units can be calculated using middle prices practised by commercial concerns. On this basis the total value of the annual output is £12.24 million. This splits as £4 million due to factors VIII and IX, £5.1 million to plasma protein fractions and the remaining £3.14 million to the immunoglobulins.

The overall contribution to NHS funds is therefore a minimum of £4.8 million and could be as high as £7.0 million according to the valuation of the input raw plasma.

Product costs at the plasma prices quoted above are given in Appendix 2.

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REVENUE EXPENDITURE

Was contained within the cash limit and is shown in Appendix 3.

CAPITAL EXPENDITURE

The greater part of the capital expenditure concerned the essential renovation of the production building, to allow production to continue until the redevelopment of the laboratory takes place and is completed. It is stressed that this expenditure can only be considered to be a temporary holding operation of short duration.

Other items are either capitalised maintenance or the replacement of worn-out or inadequate equipment.

Of note is the item of £164,000 under fees which would not be encountered in industry, this work normally falling under the professional competence of the employed engineers and technical director.

A main breakdown of the interim building projects follows, and a cost breakdown for the year is given in Appendix 4.

FEASIBILITY STUDY

At the first meeting of the Policy Steering Group for the redevelopment of BPL on 9 September 1981, the Director, BPL, was instructed to prepare a Feasibility Study and present a report by 31 December 1981.

Six companies were therefore approached and a choice made to conduct the study in collaboration with Matthew Hall Norcain Engineering Ltd. (MHNE).

The study was discussed at a December meeting of the Policy Steering Group with MHNE. It demonstrated that redevelopment of the BPL on the Elstree site is feasible, to give a plant capable of processing 500 tonnes of input plasma per annum.

A final decision to go ahead with the next phase of the project is awaited.

The cost of the study was £33,100 plus VAT.

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INTERIM BUILDING PROJECTS

Pending a decision to redevelop the Laboratory, an interim upgrading programme was authorized to maintain minimal manufacturing standards, and safeguard product standards. This programme has experienced many problems and has suffered from lack of adequate direct management.

MARP 01 LARGE FRACTIONS (400B/156 NMT RHA Ref)

Initial phases covering Inspection, Packing and Dispatch and Final Solutions areas are now completed and reoccupied. The project was extended to include stepover facilities for Final Solutions, formerly part of L.F. Stepover project 400B/160.

Technical Services and final phase work commenced on 19 April 1982. Some necessary variations from the original specification have been dealt with and the project is now some weeks behind schedule, with probable completion July 1983.

MARP 03B COAGULATION FRACTIONS (400B/158)

Improves the manufacturing area and installs new equipment. Project began 26 May 1982 and was for 28 weeks duration; nearing completion now, it is 18 weeks behind schedule.

Complexity of the project has overwhelmed the main contractor, who has not exercised control over sub-contractors satisfactorily. Much work has required to be redone; and specification shortcomings have also been encountered.

GLYCOL PLANT UPGRADING (400B/157)

Adds a third chiller to the existing 10 year old pair and reinsulates in the plant room, includes some builders work to improve area and control noise. Project performed in piece meal fashion to avoid loss of facilities. Was started in 1980/81 and was virtually completed during major shut-down from 3-15 March.

PYROGEN FREE WATER STILL REPLACEMENT (400B/159)

Introduces a Finn Aqua still into the laboratory system and relegates the existing stills to standby function. Some preliminary work carried out before main contract which began on 19 January for four weeks. Commissioning of still and treatment plant is delayed due to additional requirements.

NORTH SITE HEATING (400B/162) phases 1, 2 & 3

To replace a condemned boiler, include Queensberry Lodge and provide treated water to the plant. Contract began 18 January 1982 and changeover was achieved 8 March. Some problems remain to clear. Phases 4 and 5 should follow in 1982/3.

PERSONNEL

Staff members are given in Appendix 7 together with a split by catergories and departments.

INDUSTRIAL RELATIONS/CONSULTATION

The year has passed without any industrial relations problems, and is a continuation of the record over the previous four years of no industrial disputes.

Credit must be given, for this achievement, to both management style, and the responsible attitudes demonstrated by the staff and their representatives.

In the last quarter a local consultation committee, (LCC), was set up at Elstree, subordinate to the Joint Consultation Committee, (JCC), and empowered to deal with matters relating purely to the site. A similar arrangement was created at Oxford. The net result of these sub committees, has been to delete purely domestic matters from the JCC agenda, freeing the JCC to consult on items of wider import.

The programme of JCC meetings has been left at six weekly intervals for the time being, until it becomes clear whether a longer interval is more appropriate. Between JCC's three LCC meetings are normally held.

TRAINING

Management training workshops initiated in the early part of 1981 were extended in October to second and third line managers. These consisted of a series of eight sessions over the period November 1981 - March 1982 covering disciplinary procedures; the role of the manager, current employment and safety legislation; communication; recruitment and selection; staff training and development; and management leadership.

A further extension to include supervisory staff has now begun which will continue through 1982. Refresher courses are planned for 1982/83 in the light of changes in current employment practice and industrial relations.

The ability to hold the workshops has been enhanced by the development of an Audio-Visual Aids Unit through purchases of a film projector. Films have been available through the Training Section of North West Thames Regional Health Authority and the C.O.I.

As part of the overall staff training programme, several educational visits were organised with North London Blood Transfusion Centre. Through this, staff from the Laboratory were able to understand the wider implications of blood transfusion, and the role played by the National Blood Transfusion Service in the development of the Blood Products Laboratory.

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INTERNAL RELATIONS

(a) Staff Induction

A comprehensive induction training programme was introduced in July 1981 for all new appointments. The objective of the programme is to ensure that all essential action takes place to integrate the employee into the organisation by providing the information and training necessary to obtain effective performance from the new employee at the earliest opportunity.

A "Welcome" folder is given to all new employees on their first day, followed by a programme of induction using "checklists" for use by line-managers. within the first two months of employment, all new staff attend a formal one-day "off-the-job" course which highlights the importance of the product; Health and Safety; and Good Manufacturing Practice. A follow-up interview between the employee and his manager is held at three months.

It is proposed to extend formal induction training in 1982/83 to cover the further training development of the employee in the year following the appointment.

(b) Communications

Defined lines of communication within the laboratory, brought about by the re-organisation of key personnel have been established.

A quarterly house newsletter, "Grapevine", is issued to all staff, updating the latest information on building projects, long-term management policies, and general news and reviews. Staff are encouraged to submit articles for inclusion.

(c) Information

During 1980/81, lunchtime Seminar Clubs were held for those staff wishing to attend, to hear a series of talks given by laboratory managers on a wide range of topics covering all aspects of blood fractionation technology. In 1981/82, three further seminars were held, in which the Club heard visiting speakers from allied industries and the Health Service.

Further seminars are planned for 1982/83.

EXTERNAL RELATIONS

(a) Suppliers

During the year, several staff visited manufacturers of goods and services to BPL, as part of an on-going requirement for access to new developments and new technology.

(b) The Transfusion Service

Over the year, contacts have been maintained with users of BPL products through the Regional Transfusion Centres. Apart from the normal contacts associated with production, the programme of visits to RTCs begun in 1980/81 was continued through 1981/82 by the Director and several senior staff. Formal lectures with slides were given by the Assistant to the Director at Sheffield RTC and Cambridge RTC on the work performed at BPL and, in particular, on fractionation yield data as it affected pro-rata.

(i) Pro-rata return of product

As part of the pro-rata agreement, production data is sent to RTDs on a monthly basis. These returns show current production yields for each Centre's plasma input, and the balance between fresh frozen plasma (FFP) input and time-expired plasma (TEP) input, the objective being to increase FFP and reduce TEP collection.

(ii) Market survey of albumin products.

In November 1981, all Regions were requested to advise BPL on the likely demands of salt-poor albumin and paediatric PPF during 1982/83. Replies received indicate that a threefold increase in production of paediatric PPF, and a twofold increase of salt-poor albumin was required at BPL to meet with their forecast demands.

(iii) Visits to the Laboratory by Regional staff

Visitors to the Laboratory from within the Service were encouraged during the year. As part of the continuing training programme, Senior Registrars from North London, South London, and North East Thames Centres visited the Laboratory in July, August and February. Their programme included talks with senior staff; an explanation of BPL and its products and a tour of the production areas. In September, the Southern Area Regional Donor Organisers spent a similar day at the Laboratory.

These visits play an important role in maintaining a close liaison with the Transfusion Service.

(c) Community Relations

The wider aspect of community relations was also extended during 1981/82. the main objective was to inform the community of the functions of BPL and to educate propective employees, so aiding recruitment.

To this end, a great deal of effort was aimed at the local press; the local school's careers staff and community groups, such as the Round Table and Inner Circle. Several youth groups were also visited during the year.

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Information articles placed in the scientific press generated a large response of enquiries within the Health Service. Enquiries from the general public on aspects of blood transfusion therapy were also dealt with.

Senior staff were also involved within the higher education sphere, in the training of students for Institute of Medical Laboratory Science examinations at several Technical Colleges, thereby influencing such bodies to include, within their syllabus, material on the fractionation processes. An IMLS symposium on Blood Products, including speakers from the Laboratory, was held at Cambridge in April 1981.

The BPL was also represented at a local school's careers convention, which also included many local employers. Advice and information on careers within plasma fractionation was given to teachers and school-children alike.

Throughout the year, several community leaders visited the Laboratory, including a party of MPs; the Under-Secretary of State, Mr. G. Finsberg; and the Chairman of North West Thames Regional Health Authority, Dame Betty Paterson.

OXFORD LABORATORY

CHANGES IN STAFF AND MANAGEMENT STRUCTURE

The retirement of Ethel Bidwell as Head of Laboratory on 31.7.81 necessitated a major revision of the management structure for this section of BPL.

On Dr. Bidwell's retirement Dr. Snape was appointed Acting Scientist in Charge reporting to the Director, with Dr. Smith continuing his role as Head of Coagulation Factor Production for both the Oxford and Elstree sections of BPL. Dr. Snape's subsequent appointment (effective 1.2.82) as Head of Quality Control necessitated further reorganisation. At the time of writing an effective Senior Management presence at PFL is maintained by the attendance of Mr. Mallory, Dr. Smith and Dr. Snape at PFL for a joint total of approximately five days per week.

Coagulation factor production and development at PFL may now be considered an extension of the Elstree operation, with the Assistant Scientist (Production), PFL, David Evans, reporting directly to Dr. Smith. Similarly, the PFL Control Section now operates as one of six units of the BPL Control Laboratory, with the Assistant Scientist (Control), PFL, Geoff Sims (appointed 1.1.82) reporting to Dr. Snape as Head of Quality Control. This arrangement is facilitated by the extensive experience of both Assistant Scientists in their own area (albeit as members of the technical staff). Other sections of PFL (administrative and technical support) report directly to Mr. Mallory.

DEVELOPMENT PROJECTS

Clinical Trials

The report of that section of the trial on use of Factor IX concentrates in conditions other than Christmas disease dealing with a comparison of the use of whole plasma with the use of concentrate to treat patients before liver biopsy has been submitted to the Medical Research Council's Committee on Blood Transfusion Research.

The report on the second part of the trial concerning the treatment of patients requiring rapid reversal of anticoagulants is now complete and ready for submission.

Assay of Factor VII

The Factor VII concentrate type 7D is now routinely assayed by a coupled amidolytic clotting assay. Data currently available indicate a clotting to amidolytic ratio of 1 for all preparations, suggesting freedom from activation of Factor VII. In fact the return of higher values in the amidolytic assay is a cause of some concern and possible causes are being investigated.

Stability Studies

Data from on-going stability studies of all three Oxford products have now been analysed and indicate greater stability for all products than could have been expected. A proposed alteration to the Factor VII product licence has been agreed by Medicines Division (Licensing) in which the expiry date has been increased from one year to two at +4C. Data from the stability studies would suggest that all three products could be stored for at least one year at high ambient temperature (20-30C) with less than 10% loss of activity.

Fibronectin

Work has begun to produce a therapetic fibronectin concentrate using the cold precipitate fraction currently discarded during the Factor VIII process.

Plant

Plasma thawing machine

Development continued on this machine to the point where two 75 kg batches of plasma (unsuitable for fractionation use) were successfully thawed. Work on this machine was suspended in favour of the development of the plasma crushing machine. The first full run using plasma, recovering cryoprecipitate and then Factor IX from the cryosupernatant, has been satisfatorily completed.

Bag Opening Machine

This novel machine has been designed to remove the top of frozen "wedge" packs and then remove the plasma. The machine has been wholly built in the PFL workshops.

Plasma Crushing Machine

This machine has been developed to the point where it will efficiently crush single-donation Fenwal or "wedge" packs at a rate of greater than 1200/hr. It is hoped that it will shortly be introduced into the production schedule following minor modifications to its construction and control unit.

DHSS Inspection

The premises were formally inspected on 23/24th June, 1981 by Mr. K. J. Ayling and Mr. D. Haythornthwaite, and a report subsequently submitted to the Director for comment. Most of the recommendations made by the Inspectors have now been implemented, the rest will be acted on in the year 1982/83.

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Alterations to Building in accordance with Medicines Inspectorate recommendations

(1) Completion of entry Room to Clean Areas

The constructions of a small room to act as a changing room for members of staff entering the Clean Processing Areas was finally completed during the early part of the year.

(2) New Offices

The original workshop has been converted into two offices, allowing paper handling operations to be excluded from the Clean Processing Area.

(3) Workshop

A refurbished area for both the electrical and mechanical workshops.

(4) Testing for Sterility ("TFS") Room

The room in PFL annexe has been fitted with a bench and laminar flow cabinet. Inspection and Labelling are now performed in a quieter area, providing greatly improved product security.

PRODUCTION

Oxford production is included together with Elstree production in the appropriate appendix.

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A SECTION OF THIS DOCUMENT HAS BEEN REMOVED

TO THE FILE CONTAINING TECHNICAL AND

SCIENTIFIC DOCUMENTS SUBJECT TO RESTRICTIONS

ON INSPECTION AND COPYING SET OUT IN THE

ORDER OF MR JUSTICE OGNALL ON 8TH MAY 1990

Input

Fresh Frozen Plasma processed	116,228 kg
Total Plasma processed	138,230

Output (Released)

Product	Dose	Units
Plasma Protein Fraction (PPF)	100 ml	2,665
"	400 ml	152,793
Salt Poor Albumin 20%	100 ml	6,028
"	25 ml	9,000
" 10%	100 ml	284
Normal Immunoglobulin	250 mg	97,595
"	750 mg	50,515
"	15 mg	1,225
Specific Immunoglobulins		
Anti-D	500 g	1,010
	100 g	68,220
	50 g	42,795
Anti-tetanus	250 iu	23,020
Anti-HBsAg	500 mg	5,520
	250 mg	590
	100 mg	4,220
Anti-varicella	250 mg	5,710
	50 mg	470
Anti-rabies	500 iu	3,560
Anti-vaccinia	500 mg	1,000
Factor VIII	250 iu	86,101
Factor IX	600 iu	19,835
Fibrinogen	2 g	173
	500 iu	367
	1,000 iu	-
Accredited donor fibrinogen	175 mgs	300

Note that output figures are not to be related to input quantities, due to the existence of intermediate stocks and the length of the production process

BPL & PFL PRODUCT COSTING 1981 INCLUDING RAW PLASMA

	BPL/PFL Process Cost	Raw Plasma	TOTAL
	£ p	£ p	£ p
PPF 400 ml	7.63	6.65	14.28
100 ml	7.90	1.71	9.61
Salt Poor Albumin 20g%	8.23	7.60	15.83
10g% Albumin Sol. 2.5 ml	.73	.09	.82
" " " 10.0 ml	14.40	.38	14.78
Normal Immunoglobulin 250 mgm	1.49	5.00	6.49
" " 750 mgm	2.02	15.00	17.02
Anti-D 2500 i.u.	2.87	2.95	5.82
" 250 i.u.	1.25	.28	1.53
" 500 i.u.	.99	1.05	2.04
Anti Tetanus 250 i.u.	9.53	3.84	13.37
Anti HB 500 mg	4.56	.77	5.33
" " 250 mg	8.46	4.15	12.61
Anti Varicella Zoster 250 mg	7.70	4.17	11.87
" " " 50 mg	6.36	.96	7.32
Anti Rabies 500 i.u.	6.33	2.50	8.83
Anti Vaccinia 500 mg	5.23	.75	5.98
Fibrinogen for I.L. 35 ml	189.38	Not available	
" FB 200 ml	21.44	Nil	21.44
Thrombin 500 i.u.	10.52	Nil	10.52
Factor VIII 250 i.u.	9.77	13.75	23.52
Factor IX 600 i.u.	16.70	61.50	78.20
Factor VII 500 i.u.	315.02	-	315.02

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BPL/PFL - REVENUE OUTTURN 1981/2 — Appendix 3

Expenditure:-		BPL £	PFL £	TOTAL £
Staff Costs (salaries and employees N.I. and Sup'n contributions)		1,142 790	185,446	1,328,236
Non Staff Costs				
Staff expenses (Incl Transport, Canteen, Travelling and Subsistence etc.)		63,649	3,445	67,094
General supplies		509,617	66,140	575,757
Overheads (Rates, Electricity oil, Machinery M'tence Cleaning, Admin RHA. Rent OAHA etc. etc.)		411,316	31,050	442,366
Equipment Purchases		220,274	33,307	253,581
Buildings & Estate M'tence		49,440	24,463	73,903
V.A.T.		139,055	17,922	156,977
		2,536,141	361,773	2,897,914
Less Receipts				
Rents	10,140			
Grants & Services	1,670			
Sundries	389			
RIA Tests	268,937	281,136	-	281,136
Net Revenue Outturn		2,255,005	361,773	2,616,778
Cash Limit (Adjusted by £100,000 for sales of RIA Tests and Rents etc.)		2,266,000	361,000	2,627,000

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BPL CAPITAL EXPENDITURE OUTTURN 1981-82

Appendix 4

	Contractors	Equipment	Sundries	Fees	Total
Large Fractions	192,790	35,600	180	38,420	266,990
Stepover		318		2,635	2,953
C.F.	277,775	204,209	557	78,627	561,168
Mod. Cold Store	680			3,941	4,621
Pyrogen Free Water	15,394	26,704	564	CR 76	42,586
Freeze Drying & Workshop				1,872	1,872
Hepatitis Lab	18,820	8,825	1,592	6,856	36,093
Sewage Plant				3,187	3,187
Glycol Cooling	19,902	7,266	2,594	11,111	40,873
Virology Laboratory		31,992	56	3,159	35,207
Cottages upgrading	26,546		136		26,682
Animal House Autoclave	2,920				2,920
Bacteriology Royco Counter		9,011			9,011
Fulton Boiler	32,880		567	8,104	41,551
Computer Finance Section		16,796	3,829		20,625
Tech. Serv. Autoclave & Washing Machine		66,330			66,330
	587,707	407,051	10,075	157,836	1,162,669

VAT	75,115
NWT RHA Admin Charges	4.000
CASH LIMIT	1,241,784
	1,240,000

Feasibility Study (Matthew Hall)	33,100	
V.A.T.	4,965	
	38,065	

PFL CAPITAL EXPENDITURE OUTTURN

Virtis Freezer	8,674
VAT	1,111
	9,785
	28,000
Cash Limit	

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PERSONNEL MANNING REPORT

Appendix 5

Department Unit	1981/2			Variations from 1980/1		
	Scientific Staff	Technical Staff	Others	Scientific Staff	Technical Staff	Others
Director	1 (Med)+1	-	1			
Deputy Director	2	-	1	+1	-	+1
Large Fractions	1	6	7	-	-	-
Specific Fractions	1	3	-	-	-	-
Filling & Final Solns	-	6	7			+1
Coagulation Factors	2	11	5	+1	-	-
PFL Oxford	3	17	6	-1	-	-
Quality Control	1			+1		
Bacteriology	1	11	1	-1	+1	
Control Chemistry	1	4			+1	
Hepatitis Test Lab	1	4		+1	+1	
Virology Laboratory	1	2		-1		
Technical Services		3	12			-1
Freeze Drying		2	2		-1	
Inspection, Packing & Despatch		2	10			+1
Engineering	1		6	+1		-1
Refrigeration	-	-	-			-1
Administration	3		28			+5
Research & Development	4	3		+1	+1	
Total	24	74	86	+3	+3	+5

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PUBLICATIONS 1981/82

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Appendix 7a

REPRESENTATION AT INTERNATIONAL MEETINGS

Dr. J.K. Smith	6-8 April 1981	"Self-Sufficiency" Working Party, DHSS. Brussels.
Dr. R.S. Lane	11-13 May 1981	Meeting on Plasma Collection, American Red Cross, New York. (Speaker)
Dr. G.S. Turner	2-5 June 1981	"Immunology and Rabies Vaccines, CNER/WHO Scientific Meeting. Nancy, France. (Chairman)
Dr. R.S. Lane Dr. J.K. Smith	8-9 July 1981	Haemonetics Research Institute - European Symposium on plasma resource for fractionation of coagulation factors. Montreux, Switzerland. (RSL Chairman, JKS Speaker)
Dr. R.S. Lane	10-17 July 1981	8th Int. Congress on Thrombosis and Haemostasis, Toronto, Canada. (Co-contributor) Response to infusion of polyelectrolyte fractionated Human Factor VIII in Human Haemophilia.
Dr. J.K. Smith	10-17 July 1981	8th Int. Congress on Thrombosis and Haemostasis, Toronto. (Committee)
Dr. G.S. Turner Mr. P. Harrison	2-7 August 1981	5th International Congress of Virology, Strasbourg, France. (GST Speaker, PH Poster)
Dr. R.S. Lane Dr. J.K. Smith	23 November 1981	Meeting on Developments in Separation of Factor VIII. Groningen, Holland. (RSL Chairman)
Mr. D. Evans	18-22 November 1981	Netherlands Red Cross Symposium. Groningen, Holland.

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Appendix 7b

REPRESENTATION AT NATIONAL MEETINGS

Dr. M.J. Harvey	5-10 April 1981	Second European Congress on Biotechnology. Eastbourne.
Dr. R.S. Lane Dr. J.K. Smith	20 May 1981	Travenol Seminar: "Advances in Blood Transfusion Practice". Cambridge. (RSL Speaker)
Dr. R. Brown	1-3 July 1981	Symposium: "Bioluminescence and Electrophoretic Methods". Sussex University.
Dr. J.K. Smith Dr. T.J. Snape	25 September 1981	Biotest Symposium and visit to PFC, Edinburgh.
Dr. J.K. Smith Dr. T.J. Snape	28-29 Sept. 1981	Brit. Soc. Thrombosis and Haemostasis. Leeds.
Dr. M.J. Harvey Dr. R. Brown	12 October 1981	Mutagenicity Testing Meeting.
Mr. J. Williams Mr. P. Prince	16 December 1981	Symposium at Pharmaceutical Society, London: "Hygienic Manufacture and Microbiological Quality Control".
Mr. L. Vallet Dr. M. Harvey	5-6 January 1982	Symposium: "The Monoclonal Revolution". Cambridge.

Dr. R.S. Lane served on the Biologicals Sub-Committee of the Committee on Safety of Medicines.

Dr. R.S. Lane, Dr. E. Bidwell and Mr. L. Vallet served on Committee K (Blood Products) of the British Pharmacopoeia Commission. Dr. T.J. Snape has taken Dr. Bidwell's place following her retirement.

Mr. L. Vallet attended meetings of Group 6B (Blood and Blood Products) of the European Pharmacopoeia Commission (Strasbourg) as a consultant.

ANNUAL REPORT 1981/2

Blood Products Laboratory,
Elstree, Herts.

Plasma Fractionation Laboratory,
Oxford.

R.S. LANE, MD MRCP MRCPath,
Director.

20th April 1982.

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Input of frozen fresh human plasma to BPL increased for the first time in five years; it was all fractionated to Factor VIII with only minimal losses and output of intermediate VIII concentrate and other main products increased accordingly. Concomitant with this improved production was the major disruption of the interim building refurbishment.

The laboratory and staff progressively accommodated the philosophy and practical implications of Good Manufacturing Practice and other regulatory requirements. The major design faults of BPL remain, however, and continue to exert a real compromising effect on laboratory performance and product safety. The need to define an early target date for completion of a new BPL process factory cannot be understated. BPL is now approaching capacity or above capacity in all mainstream activities from raw material supply and fractionation to quality control and research and development. Perhaps the two most oppressive shortcomings are the inability to bring on-line new products for clinical use and the lack of capacity permitting full economic fractionation of the existing resource. Thus the interim refurbishment of BPL only allows for improved product safety and production volume to a limited degree.

The next two years will see a programme of increased Regional plasma supply aimed at full use of the existing whole-blood plasma resource. This could realise between 150 and 200 tonnes of fresh plasma for fractionation. Management must understand that the greater the success in promoting Regional activities, the greater becomes the risk of stock-in failure of production at BPL.

BPL looks forward to a new permanent management which will provide the terms of reference and operating conditions needed for full economic manufacture of plasma fractions at Elstree.

R. S. LANE,
20th April 1982.

SUMMARY

1981/82 was a year of achievement through intense, if at times conflicting, activity in the laboratory: there were major production increases despite a heavy programme of building work in the production areas, and consequent GMP problems.

Important increases in released product over 1980-81 were: Factor VIII +39%; Factor IX +38%; and 400 ml PPF +36%. Product released was valued at cost at £7.6 million, of which £4.6 million represents the notional value of the input plasma. The market value of the released material was £12.25 million.

The laboratory has been strongly represented at international congresses and meetings through chairmanship, invitations to speak and in participation in committee work. (Appendices 7a, 7b)

Nine scientific papers were published by staff members, and a further one prepared for publication: (Appendix 6)

Five major research and development projects were progressed during the year, great efforts being put into the chromatographic purification of albumin and preparation of normal human immunoglobulin for intravenous use.

A wide range of collaborative research work has been undertaken, and is listed in the report.

Mr. T. Snape completed his Ph.D. thesis, and was awarded his doctorate.

Total operating costs for the laboratory were contained within the cash limit of £2.897 million. Capital expenditure at Elstree did not fall far short of the cash limit (approximately £1,000 below), despite failure to maintain the original programme of work; however, at Oxford there was a shortfall in capital spending of £18,000. This work will need to be done in the current year.

Notable staff changes were the retirements of Dr. E. Bidwell, Head of PFL, and Dr. G.S. Turner, Head of Virology. The appointments of Mr. G.E. Mallory as Deputy Director (Manufacturing/Administration) and Dr. T.J. Snape as Head of Quality Control will strengthen the manufacturing management at the laboratory. Total staff movements were contained to give a net increase of +6% and a year end total of 184 staff manning both laboratories.

PRODUCTION

Plasma intake: at 116.2 tonnes, the fresh frozen plasma intake was 26% greater than in 1980/81. In the last half year, and particularly in the last quarter, a significant quantity of this was in single donation packs. The intention is to maximise the single pack presentation as soon as possible, to gain both in raw material hygiene and identification, in line with the requirements of Good Manufacturing Practice. This change necessitates mechanical bag opening, plasma crushing and thawing, to gain in productivity and offset the extra manual handling which otherwise would be necessary. Plasma input will therefore become progressively more machine regulated and paced and significant progress in this work will be made in the current year. Time expired plasma intake in 5 litre packs has decreased slightly - 9% less.

The processing of 138.2 tonnes of plasma over the twelve months is significant in the light of the scale of operations possible, and the many interruptions to the production processes especially during the second half of the year. At 138 tonnes the laboratory suffers from diseconomies of small scale working and in many process areas carries the penalties of pilot scale working and/or manual handling. The greater throughputs planned for the near future are welcomed as they will enable the benefits of scale to be experienced in our operations.

Slippage in completion of facilities-upgrading works when units have been released to contractors on time, have caused severe disruption to many areas of production, in particular in Factor VIII and PPF units. In the former this has created a restriction of supply to RTCs which will also continue over the next few months. In the latter, lack of production has caused inroads in stocks of released material. Overall the effects on production of the interruptions have been minimised through the dedication of staff at all levels; their efforts have avoided a serious supply crisis.

From April 1981, the system of distribution of Blood Products has been one of pro-rata returns to the RTCs relative to plasma received from each. This has had the effect of stimulating regions to supply fresh frozen plasma, and in increasing quantities.

A summary of product volumes and plasma input is given in Appendix 1.

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QUALITY CONTROL

The organisation of Quality Control in the Elstree and Oxford laboratories underwent major reorganisation in February 1982, following the appointment of Dr. T.J. Snape as Head of Quality Control. Both units are now integrated as the "Control Laboratory".

A programme of documentation review has begun in both laboratory and production areas and the first round of revision will be completed in the current year. A microcomputer has been purchased and installed in the control unit, for both word and data processing, including documentation and product specification data bases.

The present staff level is 38 with three vacancies to be filled. Dr. G.S. Turner, Head of Virology, retired on 31st December 1981, and there have been no further staff additions.

In July 1981 the routine testing of the antibody content of normal immunoglobulin was taken over by the Virus Laboratory. This had been carried out previously by NIBSC, Hampstead, and at other laboratories.

Radio immune assays for hepatitis B surface antigen have been produced and supplied to all UK Transfusion Centres and some PHLS laboratories, with limited exceptions. Reagents for some 1.5 million tests have been despatched during the year, giving a total income of around £280,000.

35,711 routine tests for hepatitis B surface antigen have been carried out on plasma pools and products, with sixteen positive results. Two of these only were on products pre-release, and are the subject of investigation. The batches used 5L pool material and the sample on the input material tested as clean. It is possible that 5L pool samples are not representative of bag contents. The changeover to single donor packs with individual pack testing at the RTC's will provide greater security against this happening in the future.

European Pharmacopoeia media and test conditions for sterility testing were introduced from 1st March 1982.

Environmental testing has been extended and intensified, and this process will continue in the current year.

With reorganisation continuing, and the ongoing revision of methods and systems, the Quality Control Laboratory will make a significant input this year in our drive to improve practices and standards.

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REVENUE EXPENDITURE

Was contained within the cash limit and is shown in Appendix 3.

CAPITAL EXPENDITURE

The greater part of the capital expenditure concerned the essential renovation of the production building, to allow production to continue until the redevelopment of the laboratory takes place and is completed. It is stressed that this expenditure can only be considered to be a temporary holding operation of short duration.

Other items are either capitalised maintenance or the replacement of worn-out or inadequate equipment.

Of note is the item of £164,000 under fees which would not be encountered in industry, this work normally falling under the professional competence of the employed engineers and technical director.

A main breakdown of the interim building projects follows, and a cost breakdown for the year is given in Appendix 4.

FEASIBILITY STUDY

At the first meeting of the Policy Steering Group for the redevelopment of BPL on 9 September 1981, the Director, BPL, was instructed to prepare a Feasibility Study and present a report by 31 December 1981.

Six companies were therefore approached and a choice made to conduct the study in collaboration with Matthew Hall Norcain Engineering Ltd. (MHNE).

The study was discussed at a December meeting of the Policy Steering Group with MHNE. It demonstrated that redevelopment of the BPL on the Elstree site is feasible, to give a plant capable of processing 500 tonnes of input plasma per annum.

A final decision to go ahead with the next phase of the project is awaited.

The cost of the study was £33,100 plus VAT.

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INTERIM BUILDING PROJECTS

Pending a decision to redevelop the Laboratory, an interim upgrading programme was authorized to maintain minimal manufacturing standards, and safeguard product standards. This programme has experienced many problems and has suffered from lack of adequate direct management.

MARP 01 LARGE FRACTIONS (400B/156 NWT RHA Ref)

Initial phases covering Inspection, Packing and Dispatch and Final Solutions areas are now completed and reoccupied. The project was extended to include stepover facilities for Final Solutions, formerly part of L.F. Stepover project 400B/160.

Technical Services and final phase work commenced on 19 April 1982. Some necessary variations from the original specification have been dealt with and the project is now some weeks behind schedule, with probable completion July 1983.

MARP 03B COAGULATION FRACTIONS (400B/158)

Improves the manufacturing area and installs new equipment. Project began 26 May 1982 and was for 28 weeks duration; nearing completion now, it is 18 weeks behind schedule.

Complexity of the project has overwhelmed the main contractor, who has not exercised control over sub-contractors satisfactorily. Much work has required to be redone; and specification shortcomings have also been encountered.

GLYCOL PLANT UPGRADING (400B/157)

Adds a third chiller to the existing 10 year old pair and reinsulates in the plant room, includes some builders work to improve area and control noise. Project performed in piece meal fashion to avoid loss of facilities. Was started in 1980/81 and was virtually completed during major shut-down from 3-15 March.

PYROGEN FREE WATER STILL REPLACEMENT (400B/159)

Introduces a Finn Aqua still into the laboratory system and relegates the existing stills to standby function. Some preliminary work carried out before main contract which began on 19 January for four weeks. Commissioning of still and treatment plant is delayed due to additional requirements.

NORTH SITE HEATING (400B/162) phases 1, 2 & 3

To replace a condemned boiler, include Queensberry Lodge and provide treated water to the plant. Contract began 18 January 1982 and changeover was achieved 8 March. Some problems remain to clear. Phases 4 and 5 should follow in 1982/3.

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PERSONNEL

Staff members are given in Appendix 7 together with a split by catergories and departments.

INDUSTRIAL RELATIONS/CONSULTATION

The year has passed without any industrial relations problems, and is a continuation of the record over the previous four years of no industrial disputes.

Credit must be given, for this achievement, to both management style, and the responsible attitudes demonstrated by the staff and their representatives.

In the last quarter a local consultation committee, (LCC), was set up at Elstree, subordinate to the Joint Consultation Committee, (JCC), and empowered to deal with matters relating purely to the site. A similar arrangement was created at Oxford. The net result of these sub committees, has been to delete purely domestic matters from the JCC agenda, freeing the JCC to consult on items of wider import.

The programme of JCC meetings has been left at six weekly intervals for the time being, until it becomes clear whether a longer interval is more appropriate. Between JCC's three LCC meetings are normally held.

TRAINING

Management training workshops initiated in the early part of 1981 were extended in October to second and third line managers. These consisted of a series of eight sessions over the period November 1981 - March 1982 covering disciplinary procedures; the role of the manager, current employment and safety legislation; communication; recruitment and selection; staff training and development; and management leadership.

A further extension to include supervisory staff has now begun which will continue through 1982. Refresher courses are planned for 1982/83 in the light of changes in current employment practice and industrial relations.

The ability to hold the workshops has been enhanced by the development of an Audio-Visual Aids Unit through purchases of a film projector. Films have been available through the Training Section of North West Thames Regional Health Authority and the C.O.I.

As part of the overall staff training programme, several educational visits were organised with North London Blood Transfusion Centre. Through this, staff from the Laboratory were able to understand the wider implications of blood transfusion, and the role played by the National Blood Transfusion Service in the development of the Blood Products Laboratory.

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INTERNAL RELATIONS

(a) Staff Induction

A comprehensive induction training programme was introduced in July 1981 for all new appointments. The objective of the programme is to ensure that all essential action takes place to integrate the employee into the organisation by providing the information and training necessary to obtain effective performance from the new employee at the earliest opportunity.

A "Welcome" folder is given to all new employees on their first day, followed by a programme of induction using "checklists" for use by line-managers. within the first two months of employment, all new staff attend a formal one-day "off-the-job" course which highlights the importance of the product; Health and Safety; and Good Manufacturing Practice. A follow-up interview between the employee and his manager is held at three months.

It is proposed to extend formal induction training in 1982/83 to cover the further training development of the employee in the year following the appointment.

(b) Communications

Defined lines of communication within the laboratory, brought about by the re-organisation of key personnel have been established.

A quarterly house newsletter, "Grapevine", is issued to all staff, updating the latest information on building projects, long-term management policies, and general news and reviews. Staff are encouraged to submit articles for inclusion.

(c) Information

During 1980/81, lunchtime Seminar Clubs were held for those staff wishing to attend, to hear a series of talks given by laboratory managers on a wide range of topics covering all aspects of blood fractionation technology. In 1981/82, three further seminars were held, in which the Club heard visiting speakers from allied industries and the Health Service.

Further seminars are planned for 1982/83.

EXTERNAL RELATIONS

(a) Suppliers

During the year, several staff visited manufacturers of goods and services to BPL, as part of an on-going requirement for access to new developments and new technology.

(b) The Transfusion Service

Over the year, contacts have been maintained with users of BPL products through the Regional Transfusion Centres. Apart from the normal contacts associated with production, the programme of visits to RTCs begun in 1980/81 was continued through 1981/82 by the Director and several senior staff. Formal lectures with slides were given by the Assistant to the Director at Sheffield RTC and Cambridge RTC on the work performed at BPL and, in particular, on fractionation yield data as it affected pro-rata.

(i) Pro-rata return of product

As part of the pro-rata agreement, production data is sent to RTDs on a monthly basis. These returns show current production yields for each Centre's plasma input, and the balance between fresh frozen plasma (FFP) input and time-expired plasma (TEP) input, the objective being to increase FFP and reduce TEP collection.

(ii) Market survey of albumin products

In November 1981, all Regions were requested to advise BPL on the likely demands of salt-poor albumin and paediatric PPF during 1982/83. Replies received indicate that a threefold increase in production of paediatric PPF, and a twofold increase of salt-poor albumin was required at BPL to meet with their forecast demands.

(iii) Visits to the Laboratory by Regional staff

Visitors to the Laboratory from within the Service were encouraged during the year. As part of the continuing training programme, Senior Registrars from North London, South London, and North East Thames Centres visited the Laboratory in July, August and February. Their programme included talks with senior staff; an explanation of BPL and its products and a tour of the production areas. In September, the Southern Area Regional Donor Organisers spent a similar day at the Laboratory.

These visits play an important role in maintaining a close liaison with the Transfusion Service.

(c) Community Relations

The wider aspect of community relations was also extended during 1981/82. the main objective was to inform the community of the functions of BPL and to educate propective employees, so aiding recruitment.

To this end, a great deal of effort was aimed at the local press; the local school's careers staff and community groups, such as the Round Table and Inner Circle. Several youth groups were also visited during the year.

Information articles placed in the scientific press generated a large response of enquiries within the Health Service. Enquiries from the general public on aspects of blood transfusion therapy were also dealt with.

Senior staff were also involved within the higher education sphere, in the training of students for Institute of Medical Laboratory Science examinations at several Technical Colleges, thereby influencing such bodies to include, within their syllabus, material on the fractionation processes. An IMLS symposium on Blood Products, including speakers from the Laboratory, was held at Cambridge in April 1981.

The BPL was also represented at a local school's careers convention, which also included many local employers. Advice and information on careers within plasma fractionation was given to teachers and school-children alike.

Throughout the year, several community leaders visited the Laboratory, including a party of MPs; the Under-Secretary of State, Mr. G. Finsberg; and the Chairman of North West Thames Regional Health Authority, Dame Betty Paterson.

OXFORD LABORATORY

CHANGES IN STAFF AND MANAGEMENT STRUCTURE

The retirement of Ethel Bidwell as Head of Laboratory on 31.7.81 necessitated a major revision of the management structure for this section of BPL.

On Dr. Bidwell's retirement Dr. Snape was appointed Acting Scientist in Charge reporting to the Director, with Dr. Smith continuing his role as Head of Coagulation Factor Production for both the Oxford and Elstree sections of BPL. Dr. Snape's subsequent appointment (effective 1.2.82) as Head of Quality Control necessitated further reorganisation. At the time of writing an effective Senior Management presence at PFL is maintained by the attendance of Mr. Mallory, Dr. Smith and Dr. Snape at PFL for a joint total of approximately five days per week.

Coagulation factor production and development at PFL may now be considered an extension of the Elstree operation, with the Assistant Scientist (Production), PFL, David Evans, reporting directly to Dr. Smith. Similarly, the PFL Control Section now operates as one of six units of the BPL Control Laboratory, with the Assistant Scientist (Control), PFL, Geoff Sims (appointed 1.1.82) reporting to Dr. Snape as Head of Quality Control. This arrangement is facilitated by the extensive experience of both Assistant Scientists in their own area (albeit as members of the technical staff). Other sections of PFL (administrative and technical support) report directly to Mr. Mallory.

DEVELOPMENT PROJECTS

Clinical Trials

The report of that section of the trial on use of Factor IX concentrates in conditions other than Christmas disease dealing with a comparison of the use of whole plasma with the use of concentrate to treat patients before liver biopsy has been submitted to the Medical Research Council's Committee on Blood Transfusion Research.

The report on the second part of the trial concerning the treatment of patients requiring rapid reversal of anticoagulants is now complete and ready for submission.

Assay of Factor VII

The Factor VII concentrate type 7D is now routinely assayed by a coupled amidolytic clotting assay. Data currently available indicate a clotting to amidolytic ratio of 1 for all preparations, suggesting freedom from activation of Factor VII. In fact the return of higher values in the amidolytic assay is a cause of some concern and possible causes are being investigated.

Stability Studies

Data from on-going stability studies of all three Oxford products have now been analysed and indicate greater stability for all products than could have been expected. A proposed alteration to the Factor VII product licence has been agreed by Medicines Division (Licensing) in which the expiry date has been increased from one year to two at +4C. Data from the stability studies would suggest that all three products could be stored for at least one year at high ambient temperature (20-30C) with less than 10% loss of activity.

Fibronectin

Work has begun to produce a therapetic fibronectin concentrate using the cold precipitate fraction currently discarded during the Factor VIII process.

Plant

Plasma thawing machine

Development continued on this machine to the point where two 75 kg batches of plasma (unsuitable for fractionation use) were successfully thawed. Work on this machine was suspended in favour of the development of the plasma crushing machine. The first full run using plasma, recovering cryoprecipitate and then Factor IX from the cryosupernatant, has been satisfatorily completed.

Bag Opening Machine

This novel machine has been designed to remove the top of frozen "wedge" packs and then remove the plasma. The machine has been wholly built in the PFL workshops.

Plasma Crushing Machine

This machine has been developed to the point where it will efficiently crush single-donation Fenwal or "wedge" packs at a rate of greater than 1200/hr. It is hoped that it will shortly be introduced into the production schedule following minor modifications to its construction and control unit.

DHSS Inspection

The premises were formally inspected on 23/24th June, 1981 by Mr. K. J. Ayling and Mr. D. Haythornthwaite, and a report subsequently submitted to the Director for comment. Most of the recommendations made by the Inspectors have now been implemented, the rest will be acted on in the year 1982/83.

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Alterations to Building in accordance with Medicines Inspectorate recommendations

(1) Completion of entry Room to Clean Areas

The constructions of a small room to act as a changing room for members of staff entering the Clean Processing Areas was finally completed during the early part of the year.

(2) New Offices

The original workshop has been converted into two offices, allowing paper handling operations to be excluded from the Clean Processing Area.

(3) Workshop

A refurbished area for both the electrical and mechanical workshops.

(4) Testing for Sterility ("TFS") Room

The room in PFL annexe has been fitted with a bench and laminar flow cabinet. Inspection and Labelling are now performed in a quieter area, providing greatly improved product security.

PRODUCTION

Oxford production is included together with Elstree production in the appropriate appendix.

A SECTION OF THIS DOCUMENT HAS BEEN REMOVED
TO THE FILE CONTAINING TECHNICAL AND
SCIENTIFIC DOCUMENTS SUBJECT TO RESTRICTIONS
ON INSPECTION AND COPYING SET OUT IN THE
ORDER OF MR JUSTICE OGNALL ON 8TH MAY 1990

Input

Fresh Frozen Plasma processed	116,228 kg
Total Plasma processed	138,230

Output (Released)

Product	Dose	Units
Plasma Protein Fraction (PPF)	100 ml	2,665
"	400 ml	152,793
Salt Poor Albumin 20%	100 ml	6,028
"	25 ml	9,000
" 10%	100 ml	284
Normal Immunoglobulin	250 mg	97,595
"	750 mg	50,515
"	15 mg	1,225
Specific Immunoglobulins		
Anti-D	500 g	1,010
	100 g	68,220
	50 g	42,795
Anti-tetanus	250 iu	23,020
Anti-HBsAg	500 mg	5,520
	250 mg	590
	100 mg	4,220
Anti-varicella	250 mg	5,710
	50 mg	470
Anti-rabies	500 iu	3,560
Anti-vaccinia	500 mg	1,000
Factor VIII	250 iu	86,101
Factor IX	600 iu	19,835
Fibrinogen	2 g	173
Thrombin	500 iu	367
	1,000 iu	-
Accredited donor fibrinogen	175 mgs	300

Note that output figures are not to be related to input quantities, due to the existence of intermediate stocks and the length of the production process

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BPL & PFL PRODUCT COSTING 1981 INCLUDING RAW PLASMA

	BPL/PFL Process Cost	Raw Plasma	TOTAL
	£ p	£ p	£ p
PPF 400 ml	7.63	6.65	14.28
100 ml	7.90	1.71	9.61
Salt Poor Albumin 20g%	8.23	7.60	15.83
10g% Albumin Sol. 2.5 ml	.73	.09	.82
" " " 10.0 ml	14.40	.38	14.78
Normal Immunoglobulin 250 mgm	1.49	5.00	6.49
" " 750 mgm	2.02	15.00	17.02
Anti-D 2500 i.u.	2.87	2.95	5.82
" 250 i.u.	1.25	.28	1.53
" 500 i.u.	.99	1.05	2.04
Anti Tetanus 250 i.u.	9.53	3.84	13.37
Anti HB 500 mg	4.56	.77	5.33
" " 250 mg	8.46	4.15	12.61
Anti Varicella Zoster 250 mg	7.70	4.17	11.87
" " " 50 mg	6.36	.96	7.32
Anti Rabies 500 i.u.	6.33	2.50	8.83
Anti Vaccinia 500 mg	5.23	.75	5.98
Fibrinogen for I.L. 35 ml	189.38	Not available	
" FB 200 ml	21.44	Nil	21.44
Thrombin 500 i.u.	10.52	Nil	10.52
Factor VIII 250 i.u.	9.77	13.75	23.52
Factor IX 600 i.u.	16.70	61.50	78.20
Factor VII 500 i.u.	315.02	-	315.02

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BPL/PFL - REVENUE OUTTURN 1981/2 — Appendix 3

Expenditure:-	BPL £	PFL £	TOTAL £
Staff Costs (salaries and employees N.I. and Sup'n contributions)	1,142 790	185,446	1,328,236
Non Staff Costs			
Staff expenses (Incl Transport, Canteen, Travelling and Subsistence etc.)	63,649	3,445	67,094
General supplies	509,617	66,140	575,757
Overheads (Rates, Electricity oil, Machinery M'tence Cleaning, Admin RHA. Rent OAHA etc. etc.)	411,316	31,050	442,366
Equipment Purchases	220,274	33,307	253,581
Buildings & Estate M'tence	49,440	24,463	73,903
V.A.T.	139,055	17,922	156,977
	2,536,141	361,773	2,897,914
Less Receipts			
Rents 10,140			
Grants & Services 1,670			
Sundries 389			
RIA Tests 268,937	281,136	-	281,136
Net Revenue Outturn	2,255,005	361,773	2,616,778
Cash Limit (Adjusted by £100,000 for sales of RIA Tests and Rents etc.)	2,266,000	361,000	2,627,000

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BPL CAPITAL EXPENDITURE OUTTURN 1981-82

Appendix 4

	Contractors	Equipment	Sundries	Fees	Total
Large Fractions	192,790	35,600	180	38,420	266,990
Stepover		318		2,635	2,953
C.F.	277,775	204,209	557	78,627	561,168
Mod. Cold Store	680			3,941	4,621
Pyrogen Free Water	15,394	26,704	564	CR 76	42,586
Freeze Drying & Workshop				1,872	1,872
Hepatitis Lab	18,820	8,825	1,592	6,856	36,093
Sewage Plant				3,187	3,187
Glycol Cooling	19,902	7,266	2,594	11,111	40,873
Virology Laboratory		31,992	56	3,159	35,207
Cottages upgrading	26,546		136		26,682
Animal House Autoclave	2,920				2,920
Bacteriology Royco Counter		9,011			9,011
Fulton Boiler	32,880		567	8,104	41,551
Computer Finance Section		16,796	3,829		20,625
Tech. Serv. Autoclave & Washing Machine		66,330			66,330
	587,707	407,051	10,075	157,836	1,162,669

VAT	75,115
NWT RHA Admin Charges	4.000
CASH LIMIT	1,241,784
	1,240,000

Feasibility Study (Matthew Hall)	33,100	
V.A.T.	4,965	
	38,065	

PFL CAPITAL EXPENDITURE OUTTURN

Virtis Freezer	8,674
VAT	1,111
	9,785
	28,000
Cash Limit	

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PERSONNEL MANNING REPORT

Appendix 5

Department Unit	1981/2			Variations from 1980/1		
	Scientific Staff	Technical Staff	Others	Scientific Staff	Technical Staff	Others
Director	1(Med)+1	-	1			
Deputy Director	2	-	1	+1	-	+1
Large Fractions	1	6	7	-	-	-
Specific Fractions	1	3	-	-	-	-
Filling & Final Solns	-	6	7			+1
Coagulation Factors	2	11	5	+1	-	-
PFL Oxford	3	17	6	-1	-	-
Quality Control	1			+1		
Bacteriology	1	11	1	-1	+1	
Control Chemistry	1	4			+1	
Hepatitis Test Lab	1	4		+1	+1	
Virology Laboratory	1	2		-1		
Technical Services		3	12			-1
Freeze Drying		2	2		-1	
Inspection, Packing & Despatch		2	10			+1
Engineering	1		6	+1		-1
Refrigeration	-	-	-			-1
Administration	3		28			+5
Research & Development	4	3		+1	+1	
Total	24	74	86	+3	+3	+5

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Tuddenham, E.G.D., Lane, R.S., Rotblat, F., Johnson, A.J., Snape, T.J., Middleton, S. and Kernoff, P.B.A. (1982).
"Response to infusions of polyelectrolyte fractionated human Factor VIII concentrate in human haemophilia A and Von Willebrand's disease". B.J. Haemat. (in press).

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Appendix 7a

REPRESENTATION AT INTERNATIONAL MEETINGS

Dr. J.K. Smith	6-8 April 1981	"Self-Sufficiency" Working Party, DHSS. Brussels.
Dr. R.S. Lane	11-13 May 1981	Meeting on Plasma Collection, American Red Cross, New York. (Speaker)
Dr. G.S. Turner	2-5 June 1981	"Immunology and Rabies Vaccines, CNER/WHO Scientific Meeting. Nancy, France. (Chairman)
Dr. R.S. Lane Dr. J.K. Smith	8-9 July 1981	Haemonetics Research Institute - European Symposium on plasma resource for fractionation of coagulation factors. Montreux, Switzerland. (RSL Chairman, JKS Speaker)
Dr. R.S. Lane	10-17 July 1981	8th Int. Congress on Thrombosis and Haemostasis, Toronto, Canada. (Co-contributor) Response to infusion of polyelectrolyte fractionated Human Factor VIII in Human Haemophilia.
Dr. J.K. Smith	10-17 July 1981	8th Int. Congress on Thrombosis and Haemostasis, Toronto. (Committee)
Dr. G.S. Turner Mr. P. Harrison	2-7 August 1981	5th International Congress of Virology, Strasbourg, France. (GST Speaker, PH Poster)
Dr. R.S. Lane Dr. J.K. Smith	23 November 1981	Meeting on Developments in Separation of Factor VIII. Groningen, Holland. (RSL Chairman)
Mr. D. Evans	18-22 November 1981	Netherlands Red Cross Symposium. Groningen, Holland.

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Appendix 7b

REPRESENTATION AT NATIONAL MEETINGS

Dr. M.J. Harvey	5-10 April 1981	Second European Congress on Biotechnology. Eastbourne.
Dr. R.S. Lane Dr. J.K. Smith	20 May 1981	Travenol Seminar: "Advances in Blood Transfusion Practice". Cambridge. (RSL Speaker)
Dr. R. Brown	1-3 July 1981	Symposium: "Bioluminescence and Electrophoretic Methods". Sussex University.
Dr. J.K. Smith Dr. T.J. Snape	25 September 1981	Biotest Symposium, and visit to PFC, Edinburgh.
Dr. J.K. Smith Dr. T.J. Snape	28-29 Sept. 1981	Brit. Soc. Thrombosis and Haemostasis. Leeds.
Dr. M.J. Harvey Dr. R. Brown	12 October 1981	Mutagenicity Testing Meeting.
Mr. J. Williams Mr. P. Prince	16 December 1981	Symposium at Pharmaceutical Society, London: "Hygienic Manufacture and Microbiological Quality Control".
Mr. L. Vallet Dr. M. Harvey	5-6 January 1982	Symposium: "The Monoclonal Revolution". Cambridge.

Dr. R.S. Lane served on the Biologicals Sub-Committee of the Committee on Safety of Medicines.

Dr. R.S. Lane, Dr. E. Bidwell and Mr. L. Vallet served on Committee K (Blood Products) of the British Pharmacopoeia Commission. Dr. T.J. Snape has taken Dr. Bidwell's place following her retirement.

Mr. L. Vallet attended meetings of Group 6B (Blood and Blood Products) of the European Pharmacopoeia Commission (Strasbourg) as a consultant.

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