Witness Name: Glenn Wilkinson
Statement No.: WITN2050001
Exhibits: WITN2050002 – WITN2050114
Dated: 14 August 2020

INFECTED BLOOD INQUIRY

EXHIBIT WITN2050022

Not a DHSS Security marking...

~~CONFIDENTIAL~~

DHSS marking: Ref

Commercial - In Confidence.

HS.1A 4/4/85.

CBLA 85/20

RESEARCH & DEVELOPMENT DEPARTMENT

BLOOD PRODUCTS LABORATORY
PLASMA FRACTIONATION LABORATORY

BCA 3/14 Tabled to CBLA 004 on 27/3/85.

ANNUAL REPORT TO DECEMBER 1984
R & D ESTIMATES 1985/6

WARNINGS

Introduction

This report contains general details of the Research and Development programme which has taken place during the year January to December 1984 and follows on from the previous report.

The year has maintained the continuous process of selection and reselection of projects to meet the ever-changing demands made on the organisation through requirements for new products or modifications to existing products to improve safety and efficacy.

The outstanding example this year has been the concurrence of requirements for improved product safety due to the presence of viruses causing non-A non-B hepatitis and the Acquired Immune Deficiency Syndrome. The widely-based group of projects aimed at purifying factor VIII to enable it to be satisfactorily heat-treated to inactivate non-A non-B hepatitis viruses has provided the means to inactivate HTLV III. The new factor VIII product, VIII-Y, materialised during the summer 1984 and is now successfully in clinical trial. Patent applications on the process will be submitted by the end of March 1985. VIII-Y has increased purity by more than one order of magnitude and tolerates more heat than is being applied to any other commercial factor VIII at present on the market, i.e. 80°C for 72 hours: yields are satisfactory and will not threaten existing plans for plasma procurement by NBTS.

The VIII-Y story underlines the importance of having a widely-based active research programme from which major advances can be made with all possible speed as demand arises.

One outstanding problem now remains in repeating the success with factor VIII in the more complex area of factor IX, and a major allocation of resources to meet this end is now established. This year BPL requires factor IX which is non-thrombogenic and free from transmission of HTLV III and other viruses causing hepatitis. The current requirement is for 15M international units per annum, which at current market rates would cost the NHS between £2M and £3M per annum.

The general report follows, then there are papers; which show the estimates of expenditure for 1985/86 and the way in which it is distributed. There is finally the project index to the main report of projects. The main report of projects is confidential and is available to the Authority and its members on request. In this way its circulation will be reduced and detailed discussion on projects can be had with the Director and the Head of Research and Development.

The continuous review of project status throughout the year has resulted six projects being merged into three revised projects; fifteen new projects have been started in response to internal and external demands; six projects have been completed and a further ten projects have been held, or shelved, pending further information or changes in emphasis. Details of all projects are given in the annual R & D project report.

The major thrust of this year's programme has been in developing methods for virus inactivation, especially non-A, non-B Hepatitis viruses (NANBH). Fortuitiously the recognition that the clinical condition AIDS is initiated by infection with the retrovirus HTLV III, and the implications this had for blood products, was covered within this research remit. It is well established that almost all previously untreated patients with no prior immunity to hepatitis viruses acquire NANBH after their first one or two infusions of either factor VIII or factor IX. The infection is often apparently trivial or sub-clinical but it is feared that more serious chronic liver damage may develop in later life. Heating coagulation factor concentrates in either the lyophilised state or in protective solutions is thought to be an effective action against NANBH viruses, HTLV III and other retroviruses. Routine batches of intermediate potency factor VIII have survived heating with acceptable factor VIII yields but some loss of solubility, this parameter has been resolved by the addition of sucrose to the factor VIII concentrate. The results from three batches which have been infused into factor VIII-deficient patients are encouraging. Each subject has been followed up for one year, six months and two months respectively; recovery, half-life and clinical effect have been normal without any adverse effects. No clinical attacks of hepatitis have been recorded and to date there has been no serological evidence of hepatitis A or B, CMV or HTLV III infection, and no evidence of NANBH from liver function tests. Similar dry-heat pasteurisation regimes have been successfully applied to routine factor IX concentrates. Clinical infusions of heated factor IX are scheduled for late 1985 on the satisfactory outcome of the current dog infusion studies with respect to potential thrombogenicity. Contingency programmes are in hand for both factor VIII and factor IX should process modifications be required, these include treating the concentrates with detergents designed to disrupt retroviruses and methods of heating in solution. The clinical trial of pasteurised antithrombin III has been extended with consistent clinical efficacy and no evidence of hepatitis transmission. The first pasteurised therapeutic concentrate of factor XIII, developed at PFL, has been successfully infused into a patient.

Undoubtedly one of the most significant advances in the past year has been the development of the new 'high purity' factor VIII concentrate. The method selectively precipitates 90% of the fibrinogen and 70% of the fibronectin present in a cryoprecipitate extract, while factor VIII remains virtually quantitatively in solution. Precipitation of the factor VIII yields a product with an 8-fold increase in specific activity when compared with the intermediate potency concentrate. Furthermore, the product can be subjected to very severe heating, 70 or 80°C for 72 hours without significant loss of factor VIII activity and very little loss of solubility. This process has been rapidly transferred through pilot scale studies to successful 900k production runs. Product characteristics have remained consistent and it is expected that the new 'high purity' concentrate (8Y) will become the national product during 1985. The first batches for clinical trial were released at the end of February with a protocol designed to assess safety and efficacy together with monitoring of possible transmission of HTLV III and viral hepatitis. Further processing of 8Y on chromatographic adsorbents results in a 5-10 fold increase in specific activity. The adsorbent has a high capacity for factor VIII and with recoveries in the 80-90% region offers a clear potential application for large-scale processing.

Considerable effort has been centred on the separation and concentration of vitamin K-dependent proteins. This reflects a BPL production requirement for a method of preparing factor IX concentrate which does not involve dilution of cryosupernatant, and recognises the planned increase in production in the new manufacturing unit. The single step preparation of factors IX, II and X from undiluted cryosupernatant has been achieved using DEAE-Sepharose at the 50kg pilot plant scale. A diluted factor VII concentrate is recovered from the same chromatographic process. The process is being refined, scaled-up and its effect on other processes assessed while awaiting results from the on-going thrombogenicity trials in dogs.

Plasma quality and its effect on plasma proteins, particularly factor VIII, has been investigated. Problems associated with the operation of filtration pheresis machines have prevented a detailed assessment of filtered plasma. Preliminary results indicate a lower level of β-thromboglobulin and fibrinopeptide A than in centrifuged plasma suggesting that platelet disruption and thrombin activation are reduced during filtration pheresis. Two new machines have been installed at the Leeds and Sheffield transfusion centres and collection of samples for detailed analysis and pilot-scale factor VIII production has started. The effect of anticoagulant volume and concentration on plasma quality has been investigated in collaboration with Cambridge RTC. At low volumes of anticoagulant there was no evidence of poor mixing, factor VIII activity and total protein were not detectably different, and there was no apparent increase in protein degradation. The level of β-thromboglobulin was observed to increase with decreasing anticoagulant volumes suggesting greater platelet lysis; this effect, together with an increase in fibrinopeptide A, was more apparent in sodium citrate plasma than CPD plasma. Cryoprecipitate produced from these experimental plasmas showed no difference in factor VIII activity or fibrinogen concentration; fibronectin levels appear to be a function of the anticoagulant volume. These results, if substantiated, would reduce the volume of 5,000 donations by 240 litres, thereby allowing an increase in the plasma content of each production batch with a concommitant decrease in the amount of water, buffer and ethanol used in the manufacturing process.

Clinicians continue to express interest in the availability of fibronectin and α_1-antitrypsin. The introduction of a new process for the preparation of factor VIII (8Y) necessitates a re-evaluation of the methods established for fibronectin preparation. Notwithstanding, the principal barrier to the release of fibronectin for clinical assessment remains the lack of an acceptable reliable assay for *in vivo* function. This deficiency severely limits our capacity to investigate the pasteurisation procedure required before product release. Assay development and assessment are proceeding; a candidate for the measurement of relevant biological activity developed at Birmingham University, has been incorporated into a wor programme directed ultimately to the clinical use of fibronectin concentrate following thermal injury. The British Thoracic Association continue t maintain a keen interest in the availability of α_1-antitrypsin for replacemer therapy in emphysema. More recently we have been approached for a supply o α_1-antitrypsin for use in heart/lung transplant patients. The preparation o 'pure' α_1-antitrypsin has been achieved using Cohn fraction IV as a sour material, however, for a variety of reasons the process cannot be transferr to either pilot or full-scale production. Recognising the limitations impos by the use of fraction IV an alternative source material has been sought wi the initial objective of deriving an α_1-antitrypsin enriched concentra without detriment to the existing manufacturing process.

Following a commercial approach we have investigated the possibility preparing lys-plasminogen for use as an acylated complex in thrombolyt therapy. Source materials have been defined and the appropriate assa established. The affinity adsorbent lysine-Sepharose has been prepared at

and elution conditions selected to yield glu-plasminogen at greater than 90% purity. Conversion to lys-plasminogen has been achieved by plasmin digestion and interim analysis suggest that the product will meet specifications. The first test sample (750mg) is now undergoing assessment.

The production of reagent grade albumin from waste Cohn fraction IV has been successfully scale-up to a level which can accommodate all the available fraction IV from production. The in-house preparation of the 40L blue-Sepharose column provides a system yielding 1.4kg albumin/10h cycle. The full potential of the automated system has been achieved through the introduction of a fraction IV clarification procedure based on graded sand bed filtration. Down-stream processing has been improved by modifications to existing diafiltration and ultrafiltration systems; sterile filtration and dispensing are now routinely employed. There has been a positive reaction to the use of the basic product in automated serology and in some instances this reaction has been extended to manual serology. The level of false positives experienced in manual serology with earlier batches has been reduced and results with a whole range of blood group antibodies have been more than equivalent to the results obtained using two commercial products. Various albumin treatments have been examined with a view to improving the performance of the product in manual serology. Gluteraldehyde cross-linking to increase the level of polymeric albumin has resulted in an improved reagent according to the recent trial undertaken by the ISBT/ICSH working party. In this comparative study against commercial products the BPL reagent gained top ranking in two of the three tests. However, two trial participants experienced false positive agglutinations with the displacement technique. A quality control programme involving 'in-house' characterisation and serological assessment by the Manchester RTC has been introduced to monitor reagent consistency. The occasional sub-standard preparation prevents the launch of a reagent for manual serology, however, the basic product for automated serology will be launched, after extensive field trials, later this year.

Apart from albumin there are other reagent grade proteins derived from waste fractions of the manufacturing process, which appear to have market potential. Preparations of transferrin and fibronectin have been assessed as tissue culture supplements with positive user reaction, however, the use of Cohn fraction IV as a direct replacement of foetal calf serum has not been successful and further work is required to advance this product. There is an increasing demand for plasminogen in the assay of tissue plasminogen activators and a product, prepared from the waste fraction B+1, is currently under assessment at CAMR, Porton. Other proteins requested as reagent-grade products include fibrinogen, thrombin, immunoglobulins and modified albumin. The requirement for these products, excluding serological albumin, is largely unknown; a market survery will be initiated early this year to evaluate the potential prior to deriving a costing programme.

Personnel

Two new scientific appointments were made at the beginning of the year; r Neal was employed to investigate the chromatographic fractionation of factor VIII and was assigned responsibility for reagent grade products. The continuity of the plasma filterpheresis programmes was maintained by appointing as a project scientist to replace completed her MRC project grant in October and the department also lost the services of during the course of the year. The position of senior scientist has been filled by who comes to us with experience of both academic and industrial environments. Five new technicians have been appointed at BPL, and two replacement technicians have been taken on at PFL. has been promoted to a trainee management position at PFL, whilst and have been promoted to Senior Project Leader and Chief Technician respectively.

Building

The conversion of Building 9 to give three new laboratories was completed in late summer. The area was commissioned in September and is operating at 40% occupancy. Further staffing is, in part, dependent upon the completion of an animal house facility for the department. Additional space has been released for laboratory work by acquiring a Portacabin to serve as office space for the Head of Department and the Department Secretary; was appointed to the latter position in October.

The scheduling of the new manufacturing unit to come on stream during early 1986 has considerable implications for the R & D department especially in relation to the life time of the pilot production facility (coagulation factors) at PFL. A facility appraisal report commissioned last year examined the options available for integrating the Oxford unit onto the Elstree site. The consultants after considering the feasibility and associated costs of re-using the existing production facility recommended the alternative approach of providing a purpose-built new facility. They stressed the need for a medium-term stop gap plan which recognised the problems of accommodating the functions of the Department efficiently and acknowledged the necessary expansion of the Department's activities. It must be stressed that currently the Department is unable to offer the necessary technical and scientific support essential to the production units and that this situation is likely to continue throughout the commissioning and early years of the new manufacturing unit.

BPL/PFL RESEARCH AND DEVELOPMENT

ESTIMATED EXPENDITURE 1985/86

All estimates, derived from the individual project reports, are for the year starting January 1985.

BPL Quality Control Department	12 100 (a)
BPL Production Units	301 200 (b)
BPL Research & Development Department	566 842 (c)
Plasma Fractionation Laboratory	94 400 (d)
	974 542

Notes :

(a) Costs met from the Quality Control Department Budget.

(b) Costs attributed to R & D projects are accommodated within the Production Department Budget; they include the purchase of developmental equipment for future use in routine production together with the estimated cost of the chimpanzee study on the new intravenous immunoglobulin preparation for freedom from transmission of non A, non B Hepatitis.

Tear-down machine development (CF/04)	70 000
Haemonetics plasma pack opening machine (CF/06)	50 000
Heat-treatment ovens (CF/07)	35 000
Chimpanzee study (IgG/01)	100 000
sub-total	255 000
Project expenditure (see R & D project report)	46 200
Total	301,200

(c) A breakdown of the Research & Development Department budget is given on the page (iii).

(d) PFL estimates have been adjusted for GMP requirements and proportioned according to the efforts of Research & Development, Fractionation and Quality Control in each project, taking into account the expenses incurred in the Administration and Technical Support Groups.

BPL/PFL RESEARCH AND DEVELOPMENT

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DISTRIBUTION OF BUDGET COSTS

PROCESS £295,312

(a) Improvement of existing process ---------- £87,850
8/01; 8/02; ALB/02; EF/02; EF/03; EF/05; CF/01; CF/02;
CF/03; CF/04; CF/05;

(b) New process development ---------- £207,462
8/02; 8/05; 8/06; 8/07; 8/11; FT/01; 9/02; IgG/08;
IgG/09; CF/06; CF/07;

PRODUCT £288,250

(a) Improvement of existing products ---------- £71,400
8/03; 8/04; 8/10; 9/01; 9/03; FG/01; FN/04; 13/01;
AT3/01;

(b) Investigations on potential products

(i) Clinical ---------- £152,000
FN/01; ALB/05; AT/01; AT/23; IgG/01; IgG/02;
IgG/03; PMG/01;

(ii) Reagent ---------- £64,850
FN/02; ALB/01; ALB/34; HEP/02; SMC/01; TCS/01;
TF/01; C1q/01; PMG/02;

RESEARCH £143,050

(a) Analytical developments ---------- £56,250
FG/02; FG/04; FG/05; FN/06; FN/35; IgG/05;
IgG/06; IgG/07; LAL/01; LAL/02; LAL/03; HPLC/01;
HPLC/02; BM/01;

(b) Basic ---------- £86,800
3GA/02; 3GA/03; MM/01; PP/01; ADC/01; MAB/01; CHR/01;
COM/01;

Sub total £726,61

Research & Development Department Expenses

Administration overheads	£106,598
Equipment	£ 37,332
External Research contracts	£104,000
	£247,930

£247,9

Total £974,5

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BPL RESEARCH AND DEVELOPMENT DEPARTMENT

1985/86 BUDGET

Forecast Expenditure :

Projects (see R & D project report)	318 912	
Equipment	37 332	
	356 244	..... 356 244
Department administration/New staff	76 478	
Staff expenses	11 810	
V.A.T.	18 310	
	106 598	..... 106 598
External research	104 000	..... 104 000
Total submission		566 842

PROJECT INDEX

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(New projects are denoted by an asterisk)

Topic : Coagulation Factor VIII

Project Code — Estimated Budget : £105,562

	8/01	Simultaneous removal of alhydrogel adsorbent and cold precipitate
	8/02	Improved recovery with heparin as primary anticoagulant
	8/03	Inactivation of hepatitis viruses in concentrate
	8/04	Precipitation behaviour and discrimination from fibrinogen
	8/05	Molecular exclusion chromatography
	8/06	Ion-exchange and hydrophobic interaction chromatography
	8/07	Susceptibility to proteolytic activation
*	8/10	Chromatography on anion-exchange media
*	8/11	Anticoagulant volume : effect on factor VIII and plasma quality
	FT/01	Filterpheresis trials

Topic : Vitamin K dependent coagulation factors

Project Code — Estimated Budget : £55,000

	9/01	Inactivation of hepatitis viruses in concentrates of factor IX (II and X) and factor VII
	9/02	Improved ion-exchange and affinity chromatography of vitamin K dependent factors
	9/03	Improved concentrate of thrombin for clinical and laboratory use

Topic : Fibrinogen

Project Code — Estimated Budget : £13,600

	FG/01	Preparation for clinical and laboratory use
	FG/02	Quantitative analysis
	FG/04	Fibrinopeptide analysis
	FG/05	Fibrinolytic potential of factor VIII concentrate

Topic : Fibronectin

Project Code — Estimated Budget : £23,200

	FN/01	A potential clinical product
	FN/02	Reagent grade product
	FN/04	Fibronectin and Factor VIII
	FN/06	Degradation products - isolation, identification and quantitation
*	FN/35	Fibronectin : opsonic activity and functional assay development

Topic : Factor XIII

Project Code — Estimated Budget : £Nil

	13/01	A concentrate for clinical use

Topic : Antithrombin III/Factor XI

Project Code — Estimated Budget : £10,000

	AT3/01	Concentrates for clinical use

Topic : Albumin

Estimated Budget : £44,250

Project Code

	ALB/01	Large scale production of reagent grade material from Cohn Fraction IV
	ALB/02	Automation of large scale affinity chromatography process
	ALB/05	Recovery from pathological plasmas
*	ALB/34	Albumin : traditional and polymer-enhanced serological reagents

Topic : Immunoglobulin Production

Estimated Budget : £124,400

Project Code

	IgG/01	Development of a preparation for intravenous use
	IgG/02	Clinical trial of intravenous preparation
	IgG/03	Trial of prophylactic immunoglobulin to prevent CMV infections in CMV seronegative bone marrow transplant recipients
*	IgG/08	Anti-D immunoglobulin : acid/pepsin treated for intramuscular preparation
*	IgG/09	Immunoglobulins : evaluation of virucidal treatments

Topic : Ethanol Fractionation

Estimated Budget : £1,000

Project Code

	EF/02	Filtration of cold-ethanol supernatants using non-asbestos filter media
*	EF/05	Filtration of normal immunoglobulin using non-asbestos filter media

Topic : Coagulation Factors Production

Estimated Budget : £175,800

Project Code

	CF/01	Computer technology for plasma receipt/quarantine/batching
	CF/02	Schubert filling machine : development of a filling pump/needle assembly
	CF/03	Factor VIII production : commissioning of plasma crusher/thawing vessel
	CF/04	Tear-Down Machine : development and evaluation
	CF/05	Factor IX production : recycling and centrifugation of DE52
*	CF/06	Baemonetics pack-opening machine
*	CF/07	Coagulation factors : provision of ovens for heat treatment

Topic : Potential Products

Estimated Budget : £56,650

Project Code

	AT/01	α-1-Antitrypsin : distribution and purification by selectiv precipitation
*	AT/23	α-1-Antitrypsin : chromatographic fractionation
*	PMG/01	Lys-plasminogen preparation and production
*	PMG/02	Plasminogen : preparation of a reagent-grade product
	SMC/01	Somatomedin C, purification and assay
	TCS/01	Development of tissue culture supplements
	Tf/01	Transferrin : distribution and fractionation
	C1q/01	Isolation of complement component : C1q

Topic : Analytical Developments

Estimated Budget : £32,850

Project Code

BEP/02 Antibody to Hepatitis B surface antigen
LAL/01 Validation of LAL assay for albumin and other blood proucts
LAL/02 Chromogenic substrate test : validation for selected blood products
LAL/03 Coagulation factors : LAL tests and anomalous rabbit pyrogen tests
IgG/05 ELISA for determination of antiviral IgG
IgG/06 Antiviral/antitoxin antibody assay development
* IgG/07 Bacterial lipopolysaccharide : antibody screening
* BM/01 Screening test for B-2-microglobulin
HPLC/01 High pressure liquid chromatography : protein analysis
HPLC/02 High pressure liquid chromatography : analysis of low molecular weight compounds

Topic : Process Development

Estimated Budget : £84,300

Project Code

3GA/02 Cibacron blue-Sepharose : ligand leakage
3GA/03 Cibacron blue-Sepharose : toxicity studies
MM/01 Production of a magnetic matrix for chromatography
* ADC/01 Ampholyte displacement chromatography and chromatofocussing : plasma protein fractionation
* CHR/01 Chromatography adsorbents : comparative studies
* MAB/01 Monoclonal antibody/cell culture facility
* COM/01 Computer Applications

Topic : Concluded Projects

Project Code

8/08 Factor VIII : Chromatography in relation to ligand substitution
8/09 Factor VIII : Immunoadsorbent chromatography
FG/03 Fibrinogen : qualitative analysis
FN/03 Fibronectin : as a non-immune opsonin
FN/05 Fibronectin : assay kit development
ALB/03 Albumin : development and characterisation of serological reagent
ALB/04 Albumin : polymer enhanced serological reagent
3GA/01 Cibacron blue-Sepharose : affinity of hepatitis B particle and pyrogens
BEP/01 BPL-radioimmunoassay for hepatitis B surface antigen
BEP/03 Screening tests for markers of hepatitis infectivity
AT/02 α-1-Antitrypsin : conventional chromatographic fractionation
AT/03 α-1-Antitrypsin : affinity chromatography adsorbents
IgG/04 Immunoglobulin : evaluation of Westfalia BKA6 centrifuge
EF/01 Ethanol fractionation : concentration of factor IX supernatant by ultrafiltration
EF/03 Ethanol fractionation : filtration of albumin solutions using non-asbestos filter media
EF/04 Application of Westfalia bowl centrifuges in cold ethanol fractionation
PP/01 Distribution of plasma proteins in BPL products and waste fractions

Topic : Analytical Developments

Estimated Budget : £32,850

Project Code

	BEP/02	Antibody to Hepatitis B surface antigen
	LAL/01	Validation of LAL assay for albumin and other blood proucts
	LAL/02	Chromogenic substrate test : validation for selected blood products
	LAL/03	Coagulation factors : LAL tests and anomalous rabbit pyrogen tests
	IgG/05	ELISA for determination of antiviral IgG
	IgG/06	Antiviral/antitoxin antibody assay development
*	IgG/07	Bacterial lipopolysaccharide : antibody screening
*	BM/01	Screening test for B-2-microglobulin
	HPLC/01	High pressure liquid chromatography : protein analysis
	HPLC/02	High pressure liquid chromatography : analysis of low molecular weight compounds

Topic : Process Development

Estimated Budget : £84,300

Project Code

	3GA/02	Cibacron blue-Sepharose : ligand leakage
	3GA/03	Cibacron blue-Sepharose : toxicity studies
	MM/01	Production of a magnetic matrix for chromatography
*	ADC/01	Ampholyte displacement chromatography and chromatofocussing : plasma protein fractionation
*	CHR/01	Chromatography adsorbents : comparative studies
*	MAB/01	Monoclonal antibody/cell culture facility
*	COM/01	Computer Applications

Topic : Concluded Projects

Project Code

8/08	Factor VIII : Chromatography in relation to ligand substitution
8/09	Factor VIII : Immunoadsorbent chromatography
FG/03	Fibrinogen : qualitative analysis
FN/03	Fibronectin : as a non-immune opsonin
FN/05	Fibronectin : assay kit development
ALB/03	Albumin : development and characterisation of serological reagent
ALB/04	Albumin : polymer enhanced serological reagent
3GA/01	Cibacron blue-Sepharose : affinity of hepatitis B particle and pyrogens
BEP/01	BPL-radioimmunoassay for hepatitis B surface antigen
BEP/03	Screening tests for markers of hepatitis infectivity
AT/02	α-1-Antitrypsin : conventional chromatographic fractionation
AT/03	α-1-Antitrypsin : affinity chromatography adsorbents
IgG/04	Immunoglobulin : evaluation of Westfalia BKA6 centrifuge
EF/01	Ethanol fractionation : concentration of factor IX supernatant by ultrafiltration
EF/03	Ethanol fractionation : filtration of albumin solutions using non-asbestos filter media
EF/04	Application of Westfalia bowl centrifuges in cold ethanol fractionation
PP/01	Distribution of plasma proteins in BPL products and waste fractions

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Topic : Analytical Developments

Estimated Budget : £32,850

Project Code	
BEP/02	Antibody to Hepatitis B surface antigen
LAL/01	Validation of LAL assay for albumin and other blood proucts
LAL/02	Chromogenic substrate test : validation for selected blood products
LAL/03	Coagulation factors : LAL tests and anomalous rabbit pyrogen tests
IgG/05	ELISA for determination of antiviral IgG
IgG/06	Antiviral/antitoxin antibody assay development
* IgG/07	Bacterial lipopolysaccharide : antibody screening
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HPLC/02	High pressure liquid chromatography : analysis of low molecular weight compounds

Topic : Process Development

Estimated Budget : £84,300

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Topic : Concluded Projects

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IgG/04	Immunoglobulin : evaluation of Westfalia BKA6 centrifuge
EF/01	Ethanol fractionation : concentration of factor IX supernatant b ultrafiltration
EF/03	Ethanol fractionation : filtration of albumin solutions using non asbestos filter media
EF/04	Application of Westfalia bowl centrifuges in cold ethano fractionation
PP/01	Distribution of plasma proteins in BPL products and waste fractions

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Topic : Albumin

Estimated Budget : £44,250

Project Code

	ALB/01	Large scale production of reagent grade material from Cohn Fraction IV
	ALB/02	Automation of large scale affinity chromatography process
	ALB/05	Recovery from pathological plasmas
*	ALB/34	Albumin : traditional and polymer-enhanced serological reagents

Topic : Immunoglobulin Production

Estimated Budget : £124,400

Project Code

	IgG/01	Development of a preparation for intravenous use
	IgG/02	Clinical trial of intravenous preparation
	IgG/03	Trial of prophylactic immunoglobulin to prevent CMV infections in CMV seronegative bone marrow transplant recipients
*	IgG/08	Anti-D immunoglobulin : acid/pepsin treated for intramuscular preparation
*	IgG/09	Immunoglobulins : evaluation of virucidal treatments

Topic : Ethanol Fractionation

Estimated Budget : £1,000

Project Code

	EF/02	Filtration of cold-ethanol supernatants using non-asbestos filter media
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Topic : Coagulation Factors Production

Estimated Budget : £175,800

Project Code

	CF/01	Computer technology for plasma receipt/quarantine/batching
	CF/02	Schubert filling machine : development of a filling pump/needle assembly
	CF/03	Factor VIII production : commissioning of plasma crusher/thawing vessel
	CF/04	Tear-Down Machine : development and evaluation
	CF/05	Factor IX production : recycling and centrifugation of DE52
*	CF/06	Haemonetics pack-opening machine
*	CF/07	Coagulation factors : provision of ovens for heat treatment

Topic : Potential Products

Estimated Budget : £56,650

Project Code

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*	AT/23	α-1-Antitrypsin : chromatographic fractionation
*	PMG/01	Lys-plasminogen preparation and production
*	PMG/02	Plasminogen : preparation of a reagent-grade product
	SMC/01	Somatomedin C, purification and assay
	TCS/01	Development of tissue culture supplements
	Tf/01	Transferrin : distribution and fractionation
	C1q/01	Isolation of complement component : C1q

CONFIDENTIAL

BLOOD PRODUCTS LABORATORY

National Blood Transfusion Service

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

Telephone: 01-953-6191
Telex: 8814267

Dagger Lane,
Elstree,
Borehamwood,
Herts WD6 3BX.

4075

Our Ref:

25th July 1985

To: Regional Transfusion Directors ; England and Wales

Dear Dr

DRIED FACTOR VIII FRACTION : TYPE 8Y

It was announced at the last RTD meeting that Factor 8Y would commence issue in September 1985 at a level of 7500 vials (250 iu) per month. This level of output will not increase until the new production unit is operational. Note that for September only, the issue will be part HLH and part 8Y.

Accordingly a letter has been sent to all Haemophilia Directors and a copy is attached for your information. You will see that it is hoped that active liason between Haemophilia Centres and RTCs will result in a high proportion of Factor 8Y being given to patients most at risk to infection by HTLV III and viruses associated with Non A Non B hepatitis.

A percentage of Factor 8Y is being used in clinical trials in selected patients to determine safety and efficacy of product prior to making application for a product licence in the autumn.

If you have any comments, please do not hesitate to contact me.

Yours sincerely

For file please.

6/11

HAEMOPHILIA CENTRES ANNUAL RETURNS 1984

As you suggest I will speak to [redacted] about the possibility of obtaining earlier returns for Departmental purposes. Are you prepared to fund the extra effort which would be required to produce these figures?

I think it probably would be useful to ask the Haemophilia Reference Centre Directors how they see the latest projection of UK needs for Factor VIII. I will make enquiries about how the projected figure was proposed to make the original calculations before approaching them.

5 November 1985

Room 1025a Han Hse
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cc