RSL/AH

15th March 1979.

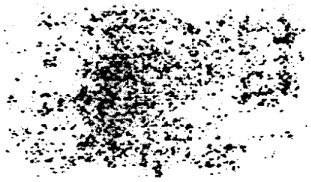
Mr. T.E. Dutton,
Department of Health and Social Security,
Hannibal House,
Elephant and Castle,
London SE1 6TE.

Dear Tom,

I have produced a document for the Scientific and Technical Sub-Committee. I hope this is the size that you require and that the production details and difficulties are not over-accentuated. I believe them to be so important that they take precedence. I am having this delivered personally by taxi so that you have an opportunity of circulating the agenda by tomorrow.

Yours sincerely,

R. S. LANE.



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The Products

A full range of products is shown in Appendix 1. The main fractions are (i) blood coagulation factor VIII prepared as a freeze-dried concentrate and used for the clinical management of classical haemophilia; (ii) purified albumin, a main protein fraction of normal plasma with many important functions including preservation of fluid balance within blood vessels: it is used clinically for its supportive effect in severe burns, in patients on intensive care and after severe injury or major surgery; (iii) normal plasma immunoglobulin and specific immune globulins: used for the containment of infections, e.g. hepatitis A, tetanus, measles, herpes etc. and the control of Rhesus sensitization of women during and after pregnancy.

Production Objectives

In accordance with WHO recommendations, BPL should produce enough plasma fractions to make the National Health Service self-sufficient. In relation to the predicted NHS requirement (DHSS Working Party on Trends in Blood Transfusion 1978-1988), actual BPL production rates and estimated maximum capacity of the existing unit are both significantly inadequate; e.g. 1979 predicted use of factor VIII approximately 60,000,000 iu; present BPL output 13,000,000 iu - maximum capacity 28,000,000 iu (cost of commercial factor VIII 10-15p/iu). Appendix 1 shows the estimated maximum capacity of BPL for all products.

The Stop Gap Programme

This is a four-year programme commencing June 1978 aimed at achieving the maximum capacity levels for products listed in Appendix 1. The various levels have been estimated in conjunction with an integrated professional work-study team; the degree of reliability of various outputs has been assessed, the main constraints and areas of concern defined; recommendations for limited development of the process in the final process areas and loading bay are being implemented.

Financial considerations To accommodate full implementation of Stop Gap, capital investment on building and equipment will be approximately £500,000; present production revenue costs are increased by £75,000 p.a. to finance additional Stop Gap production. Based on the nearest commercial equivalent valuation, pre-Stop Gap production was worth £8,000,000 p.a. - Stop Gap targets (Appendix 1) increase this output to £14,400,000 p.a. (BPL/PFL forecast budget 1979/80 £1,800,000).

Developments after Stop Gap

Within the Stop Gap period, early policy decisions are essential for the future phased redevelopment of the major laboratory fractionation/process areas. The total operation must be scaled up to realistic levels in relation to NHS needs. The Stop Gap programme is itself not a repeatable event due to the increasing risks inherent in ageing plant and fabric. Limitation on investment in BPL's phased redevelopment is a false economy since NHS must pay the commercial price for imported blood products to make good the deficiency in BPL output.

Production Systems

Source material (1978) obtained from Regional Transfusion Centres on a non-committed basis and without quality specification:

(i) Frozen fresh plasma, 67313 litres: for production of factor VIII, IX, VII, albumin, immunoglobulin.

(ii) Time-expired plasma/cryoprecipitate supernatant, 83889 litres; for albumin and immunoglobulin.

(iii) Specific immune plasma, 5711 litres; for specific immunoglobulins and albumin.

Cohn fractionation A conventional economic system for fractionation of immunoglobulin and albumin from source plasma, using increasing concentration of ethanol, decreasing temperature and pH to separate individual protein groups.

Cryoprecipitation Separation of particular proteins by freezing and controlled thawing of plasma. Cryo-globulins include factor VIII, the most important component in this fraction. Cryoprecipitation is the initial process in the separation of anti-haemophilic globulin.

Chromatographic separation Separation of protein molecules according to their size, electric charge or biological affinity, usually on columns of suitable support matrix under highly specified conditions. Examples:

(a) Anion exchange chromatography for the purification of coagulation factors IX and VII.
(b) Affinity Chromatography to separate pure human albumin (in development).

Production electrophoresis Continuous separation of protein molecules according to their electrical charge operating within an electrical field. Under development at present at the Atomic Energy Research Establishment, Harwell, in conjunction with BPL and DHSS. Possible valuable potential as an alternate form of factor VIII preparation.

GRO-C: Lane

BPL Director

March 15th 1979.

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APPENDIX 1

Specific production output objectives (Stop Gap)

P.P.F.	230,000 x 18g bottles
'Salt-poor albumin'	12,000 x 20g bottles
Fraction II paste - for anti-D diluent and as n-immunoglobulin	80,000 x 250 mg
	60,000 x 750mg
	2,000 x 15mg (for use with measles vaccine)
Albumin 10% solution	7,000 x 2.5ml
	3,000 x 10ml or 100ml
Re-precipitated albumin (10% soln.)	500 x 10ml
Factor VIII (Elstree alone) + Oxford	28.75m i.u. as 115,000 x 250 i.u.
Factor IX	7,500,000 i.u.
Fibrinogen for isotopic labelling	150 x 500mgm
Fibrinogen	2,000 x 200ml
	1,000 x 10ml
Fibrin foam	1,000 x 4 x 4cm
	300 x 2 x 2cm
Thrombin	1,200 x 100 i.u.
	1,500 x 500 i.u.
	1,000 x 1000 i.u.
Anti-D equivalent to	72,000 x 100 µg
Anti-tetanus	30,000 x 250 i.u.
Other specific immunoglobulins	20,000 vials p.a. (to include up to 11,000 chickenpox)
Whole dried plasma	up to 15,000 (includes some flexibility)

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