Section I

INTRODUCTION

1. This is the sixth Accountability Review to be prepared by the Authority and efforts have been made to shorten and simplify the report and to concentrate on the key issues.

2. Section II considers the last financial year, 1990/91 and compares performance with budget.

3. Section III considers the projections for 1991/92 and 1992/93 and highlights the key factors affecting the success of operations.

4. Section IV considers the organisational structure of the CBLA and its units BPL and IBGRL together with its relationship with the NBTS. A special report has been prepared by Touche Ross on the decoupling of BPL from CBLA. Also an assessment of the resultant status of CBLA/NBTS has been prepared by CBLA.

CHAIRMAN'S HIGHLIGHTS

I am pleased to submit herewith the Accountability Review for the past year 1990/91 and also to submit the results of our further studies on the future for BPL and its relationships with the NBTS and NHS on blood plasma and products.

During the whole of the year 1990/91 BPL was able to supply the total demand made on it for products of its own manufacture. BPL also successfully commenced direct marketing of its products and enhanced the demand. Consequently the year was a record in terms of output and achieved sales only marginally short of budget £39.3m (£39.6m). During the year manufacturing efficiencies rose and yields of Factor 8 were above the budgeted rate and at times were in excess of 200 iu/kg. As this is the lead product, costs consequently fell below budget and the gross margin was increased leaving a net surplus on trading operation of £3.4m instead of a projected deficit of £0.4m.

These results were being achieved at a time when the Authority's activities in other directions were extended to meet two new objectives as follows:

1) To get two major new products to market during the year - high purity Factor VIII (8SM) and IV IgG (Vigam). This was achieved and both products were marketed in March 1991.

2) With the removal of Crown Immunity on March 31st 1991; to ensure that all major products and premises were properly licensed and appropriate dossiers on all new products submitted to the MCA before the end of March. This objective was also achieved. This puts BPL in a strong competitive position for the 1990's.

As the two new products are currently being partly processed for BPL by Kabi of Sweden, during the coming year it will be necessary to modify the existing BPL plant and processing so that the manufacture can be transferred back to Elstree during 1991. The cost of this operation is expensive but nevertheless has been totally necessary to meet the clinical demand and for BPL to remain viable and competititive.

Clearly these activities and their success have heightened competititive commercial awareness of BPL which has prompted both press and political questions. These have been more of an irritant than a real problem for BPL.

continued/

Looking to the future, there remains two principle issues which are being addressed by a study being undertaken by Touche-Ross and by a brief assessment prepared by CBLA.

1) Because of the changing technological, economic and competitive climate, it is necessary to allow BPL to fulfil its potential as an industrial pharmaceutical manufacturer of transfusion medicine biologicals in a manner which will allow it to compete in the new European environment whilst at the same time safeguarding the independence of the unpaid volunteer plasma 'gift' which is the basic raw material of the current BPL business with the NHS (i.e. 'decoupling').

2) Suggestions are made for a revision of the relationship and status of a combined CBLA/NBTS to achieve an enhanced quality and economic supply of products from the RTC's to both BPL and other users.

It is hoped that these proposals will provide a blue print for a sound and efficient strategy and activity in future years.

A REVISED STRUCTURE AND FUNCTION FOR
THE CENTRAL BLOOD LABORATORIES AUTHORITY (CBLA)
AFTER 'DECOUPLING' BPL

Introduction

CBLA was established in December 1982 by Statutory Instrument No. 1515 "The Central Blood Laboratories Authority (Establishment and Constitution) Order 1982" to administer the Central Laboratories of the National Blood Transfusion Service (NBTS): these are BPL - now Bio Products Laboratory - and IBGRL, the International Blood Group Reference Laboratory.

By 1988, BPL had been rebuilt and commissioned and in 1990/91 the new plant received a Manufacturer's Ordinary Licence, and a Special Products Licence. The full product range was licensed in accordance with directives from the Medicines Control Agency (MCA) and in compliance with the Medicines Act 1968, the National Health Service and Community Care Act 1990 and in the light of the termination of Crown Immunity on March 31st 1991.

Also in 1990/91, BPL sales of product met all NHS demands and in so doing matched the budget sales plan for the year. By the year-end, a full portfolio of high quality products derived from human plasma had been issued for sale: future additions to the product list will come from improvements to factor IX formulation and potential substitutes for whole blood.

From this currently satisfactory operational base, CBLA and BPL management have recommended that an alternative status for BPL other than direct linkage with NHS is desirable if BPL is to fulfil its future commitments in competition with a predominantly commercial field based mainly from the USA but also in Europe. An early separation of BPL from CBLA to permit development of BPL's future status leaves the CBLA and the linkage with NBTS in equally urgent need of redefinition.

THE 'GIFT' RELATIONSHIP

Previous considerations on privatisation of BPL in 1982 were premature: the major matter of concern which surfaced during the review was the importance of protecting the Gift Relationship which exists between the voluntary unpaid blood donors, the Transfusion Service and patients. Overt commercialisation of blood or its main derivatives (notably plasma) is both unacceptable to voluntary donors and politically sensitive.

In order that the de-coupling arrangements for BPL can proceed and yet the donor's Gift be preserved from any commercial risk or stigmatisation, it has been proposed that CBLA become the custodian and administrator of the plasma resource (and any other such blood derivatives that may be fractionated e.g. haemoglobin) on behalf of the NHS and in contract with BPL. At the same time BPL can be given the opportunity to broaden and develop its business base in the light of new technology and overseas markets.

Thus CBLA will interact in both directions, the NBTS and BPL, but it is self-evident that CBLA's natural affiliation will be more with NBTS in that both parties will remain within NHS and neither will be promoting commercial aspects of blood transfusion practices.

In proposing how CBLA should be restructured, the interface with NBTS is worth particular attention in the following respects:

1. The need co-exists for changes in direction for operational management of CBLA and NBTS - the latter at national level.

2. CBLA, in its revised role, presents the opportunity to combine with the national responsibility and objectives of NBTS and avoid duplication.

3. The development of more coherent national structure for NBTS would facilitate CBLA's plasma brokerage to BPL.

4. Financial arrangements to deal with the high oncosts believed to be inherent in the voluntary blood donor programme which will require resolution by CBLA/NBTS with DoH.

ROLE FUNCTIONS FOR CBLA

The primary role for CBLA is to acquire and be custodian of the plasma 'Gift' from the voluntary donors through its processing cycle to the point of re-entry into the NHS as therapeutic products.

Inherent in this role is the security, preservation of the quality and economic utilisation of the 'Gift' in its transit from NBTS, the collection agency, to BPL, the contract fractionator.

In practice, CBLA will hold the plasma in bond.

The important element in this CBLA/NBTS role is to establish the basis of provision of plasma as a by-product of blood collection to link into the requirements statutorily defined by product registration with MCA and under EEC guidelines.

Therefore CBLA/NBTS will:

- establish procedures and resources to ensure that plasma quality meets defined standards set out in the Plasma Specification in product registration files.

- ensure by the process of audit that quality procedures in plasma collection and testing are followed and are reviewed as necessary.

- ensure that plasma supply targets are reliably met in all specified plasma types.

- work to achieve maximum efficiency in plasma collection to reduce costs.

- agree contribution to collection cost price targets with Transfusion Centres.

- carry out proper accountancy of the plasma inventory in volume and financial terms.

- report as necessary on the utilisation of the Gift.

In relation to BPL

- CBLA will contract with BPL to effect fractionation of voluntary donor plasma to a defined range of plasma derivative products.

- CBLA will contract with BPL to effect distribution and sales of the defined products in accordance with Statutory Instruments governing priority of supply to NHS.

- In accordance with management and title of the plasma 'Gift', **CBLA will own both plasma and products** and will cover product liability.

- **CBLA will be the Product Licence holder** for UK donor plasma products. However, BPL can acquire product licence variations for plasma derived from other sources.

- CBLA will require that BPL manufacture products in accordance with the Product Licences.

- CBLA will undertake quality audit of BPL as necessary.

- CBLA in contract with BPL will agree the financial management arrangements and set out the procedures for accountability and financial audit.

- CBLA will undertake with BPL that these products are presented for sale in a form and at a price which is competitive with commercial products and promotes their ready sale to the NHS.

To perform this pivotal role between Transfusion Centres and BPL, it is imperative that CBLA/NBTS is granted the statutory responsibility to guarantee optimal use of the plasma 'Gift'.

Additional CBLA/NBTS functions and liaisons:

- Report on an agreed basis to DoH/NHS executive.

- Promote voluntary blood donations and inform the donors of the use of their plasma gift.

- Maintain due contact with EC institutions managing unpaid voluntary donor systems.

- Support BPL in its promotion of CBLA products to clinical users.

- Liaise with BPL on regulatory and pharmaceutical requirements.

NBTS/CBLA OPERATIONAL RESOURCE REQUIREMENTS

Quality -	Specification Standards Accreditation and audit Systems and procedures and practice
Regulatory -	Registration and amendments: UK and EC Pharmacopoeia
Financial -	Internal CBLA/NBTS accounts Accountancy and audit Management systems
Legal -	Liability and insurance Contracts: sale and supply Patents.

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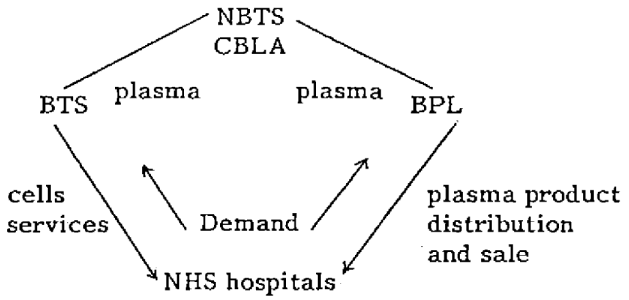
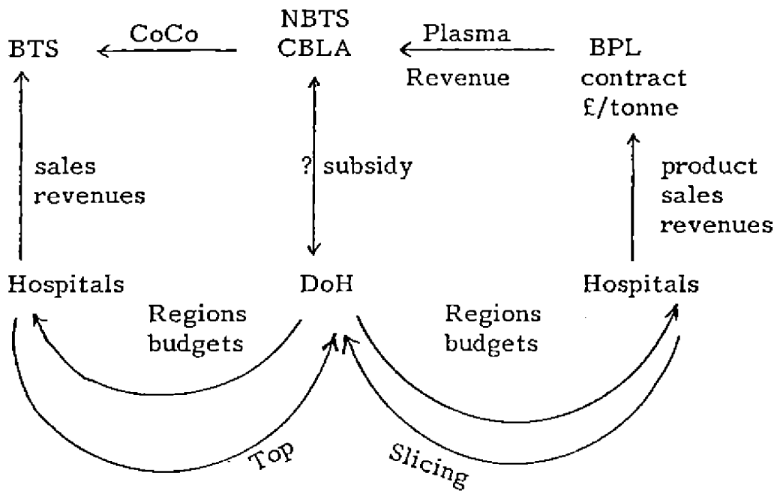
SUPPLY CHAIN



FINANCIAL MODEL



CBLA STRUCTURE

It is obvious from the Financial Model that management overheads for NBTS, CBLA and BPL should be minimised and particularly avoid duplication.

From the operational resources centres it is clear that BPL have already developed manpower resource capabilities and capital facilities in which CBLA have a direct interest.

As part of the Agreement with BPL, CBLA should contract to use specified Quality, Materials Management and Data Management functions and have access to facilities for inventory (plasma and products) and to other disciplines i.e. R & D on an agreed basis.

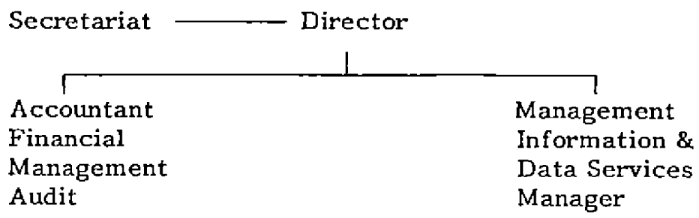
CBLA will require manpower in areas defined below to assure that contracted work is properly specified, performed and accounted for.

CBLA manpower, while drawing substantially on BPL operational resources, will also have equivalent interactions with NBTS where the specified disciplines are currently variably represented at the fourteen Regional Centres.

In its pivotal role between BPL and the regional BTS, CBLA/NBTS has a major opportunity to co-ordinate and implement practices which are based on regulatory definitions.

This co-ordination would be infinitely improved if it dealt with a nationally based Service.

CBLA MANPOWER



POSSIBLE TERMS OF REFERENCE FOR CBLA

On behalf of the Secretary of State for Health to

1. manage the unpaid voluntary donor plasma resource in accordance with Statutory requirements

2. be responsible for proper and efficient use of the plasma resource and for its safe keeping

3. arrange for fractionation of plasma derivatives in a manner best suited to the needs of NHS clinicians and patients

4. maintain full accountability for the plasma resources and its related financial transactions

5. undertake other duties as may be directed by the Secretary of State.

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THE SUBSUMING OF CBLA/NBTS INTO NATIONAL POLICY DIRECTION AUTHORITY FOR ALL ASPECTS OF BLOOD DONATION, TRANSFUSION AND USAGE

A delegated basis for operational management of blood banks is self-evident considering demographic variations in the UK and disposition of specialist clinical centres which have evolved naturally rather than in a planned manner.

The clustering of clinical centres creates a service demand which is best administered locally due to inherent market variability.

However, the existing regional distribution of fourteen main centres in England and Wales is historical. The status and practices of many RTCs have been personally characterised by individual director/managers. Thus regionalisation has ensured the Service operates at variable standards in quality and procedures, in fact it has encouraged individualism in operational practices at the expense of economy and efficiency.

While individualism may be good in some respects, important matters relating to quality, supply and financial administration have frustrated the implementation of nationally derived policies. These national requirements are increasingly defined by Statute (UK and EC) and the withdrawal of Crown Immunity now exposes the Service to levels of liability and compliance it cannot ignore.

The awareness of the national elements of policy for the Service long preceded the redevelopment of BPL. In 1974 the Reid Report drew attention to the need for central aspects of management for NBTS - but was rejected. In 1978, NBTS evidence to the Royal Commission on the Health Service repeated the need but was rejected again. In 1982, CBLA with the Consultant Advisor on the NBTS to DHSS repeated the request but without success.

The continued absence of national direction has resulted in a chronic buildup of a backlog of defects in NBTS. The recent non-executive establishment of the NBTS Directorate paid lip service to the central needs of NBTS but the absence of means of enforcement has made the Directorate's function less than effective.

Thus, executive management of RTCs resides at RHA level. **However, the position and relevance of the RHA in the supply chain of blood services to hospitals has been diminished by the new Health Act which places purchasing decisions and budgets with District Authorities and individual hospitals and removes the RHA as a primary provider.**

RTCs will increasingly derive operational revenue from sales of goods and services and in this respect it is entirely appropriate the regional or zonal blood banks should have a form of 'Trading Status' to enable a degree of competitiveness to improve market economies to the NHS.

In budget terms, RTCs will require capital financing but not revenue budgets.

In the current situation, the traditional deficiencies in the NBTS, which should be collectively managed by 'nationally standardised policy and procedures', come sharply into focus. The Transfusion Service now critically requires a statutory National Directorate capable of

- improving the Donor P.R. base

- providing coherent national representation in E.C.

- providing a defined axis for uniform national implementation of Statutory Directives (UK and EC)

- integrating national service demand and optimising the logistical means to resolve competing pressures on supply

- introducing a sound basis for financial comparability, cost and pricing structure

- introducing efficiencies, effecting cost reduction and managing audit

- managing quality programmes and Blood Bank accreditation

Delegated Blood Banks would retain

- local responsiveness to local demand

- individual accountability

- local operational management

- maintain a service base commensurate with the trading status of new hospitals etc.

- **implement national standards, policies and procedures.**

THE POTENTIAL INPUT FROM CBLA

CBLA as custodian of the Plasma Gift would arrange contract manufacture of products with BPL. The relationship with BPL would be clear-cut and stands to benefit substantially from application of the principles of the Value Managed Relationship (VMR).

Initially, CBLA/NBTS would need to contract individually with delegated RTC units where variability in national quality standards exists and where no national price structure is agreed.

An early move is advocated whereby CBLA/NBTS incorporates implementation of policies and functions which are statutorily defined or related to quality and financial policy. In dealing with blood banks, it should then be possible to establish uniform quality and accounting procedures first in association with plasma collection then as a co-ordinated application to all services.

Reorganisation of the existing regional structure of the Service into more manageable and accountable operational units which could be Trusts or Trading Fund Agencies would also follow.

CBLA/NBTS initial areas of responsibility should embrace

- Organisation
  - financial policy
  - capital allocations
  - negotiation of subsidies
  - Quality Assurance
  - national policies and procedures
  - management information services

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- Management of the Plasma Resource
- Interactions with DoH/NHS Executive
- National representation in Europe
- National P.R.

Incorporation of these management roles into CBLA/NBTS could be phased:

Residual CBLA Role	Plasma Resource/BPL Contract IGBRL
Phase I	CBLA -> NBLA National Blood Laboratories Authority or National Blood Resources Authority Divisions: Blood Bank Services National Fractionation Resources and Control IBGRL European Regulatory Affairs European Blood Resources
Phase II	NBLA -> UKBLA by incorporation of Scotland and Northern Ireland as a Division.

No views are offered on timescales except that CBLA's function to safeguard and manage the plasma resource will be increasingly jeopardised by delay in introducing executive management to the BTS at the national level.

NBLA management requirements in Phase I would be accommodated by

* Chairman and non-executive members (5)
CEO
Directors of Divisions
- Medical + Research and Development
- Operations Technical and Regulatory
  Fractionation Resources
  Planning
- Finance and Administration
- Commercial including P.R.

* Propose the 6 non-executive members one of whom would be the Chairman should represent:

1) Head of one of the major medical institutions e.g. Royal College of Physicians.

2) Senior executive from a financial institution

3) Senior Legal executive

4) Representative from RHA.

5) Two senior industrialists with experience of:

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5.1 major logistical and consumer orientation (e.g. distribution).

5.2 major scientific and research based industry (e.g. pharmaceuticals).

THE PLASMA RESOURCE FOR FRACTIONATION

Introduction

CBLA have asked for information on plasma collection and its use in fractionation to be set out in a paper which can augment proposals being prepared by Touche Ross on the future entity status of BPL and CBLA.

As a preface to the paper, is an attached leaflet prepared and distributed by the Mersey Regional Blood Transfusion Service, giving general information to donors on how blood is processed by the NBTS for use in the NHS. The leaflet indicates that plasma can be separated from whole blood and used by the fractionator to prepare a number of life-saving derivatives: these activities are described in more detail in the sections that follow.

TERMINOLOGY

Plasma, an aqueous solution of proteins and salts in which are suspended the cellular elements of blood, has been used therapeutically for over fifty years. Plasma water and its principal constituent protein, albumin, maintain normal circulatory volume without which, shock rapidly develops. In the 1940's, trauma from war wounds accelerated interest in plasma and its fractionated principle - albumin for emergency life support and the pioneering work of E.J. Cohn in Harvard established the biochemistry and chemical engineering parameters for the fractionation industry.

Although plasma has therapeutic efficacy on its own, it must be preserved either frozen or freeze dried, whereas fractionated albumin solutions are stable in liquid form: in addition, while plasma retains blood group specificity and was shown at the outset of its use to transmit hepatitis, albumin has no blood group characteristics and can be sterilised by pasteurisation.

Based on Cohn's work in the 1940s and 50s, a major industry developed, mainly in the USA, to collect plasma and prepare therapeutic derivatives, albumin and immune globulin. The industry was regulated according to the pharmaceutical standards set by FDA.

In the 1960s it was found that a protein fraction rich in anti-haemophilic globulin (factor VIII) could be separated from plasma by cold precipitation. Known as cryoprecipitation, this step was rapidly incorporated into the fractionation process at industrial scale. Later the other anti-haemophilic globulin, factor IX, was identified and incorporated into the industrial process.

By the 1970s the fractionation industry had its main product lines established:

Albumin
Immune globulin (both normal pooled and specific)
Factor VIII
Factor IX.

Except that immune globulins were developed for intravenous injection during the 1980s and there have been some process modifications, the industry has retained these main product lines from plasma for some 20 years. Also, during this time, process yields of these products have remained relatively constant, with only short-term fluctuations.

Plasma nomenclature

All plasma is supplied frozen at below -20°C.

Plasma frozen to below -20°C as soon as possible and not later than 24 hours after donation is called Fresh Frozen Plasma (FFP).

FFP is supplied in two main forms:

RECOVERED - this is plasma collected by centrifugal separation from whole blood or other cellular components (platelets)

SOURCE PLASMA (HUMAN) (SPH) - plasma collected by apheresis (plasmapheresis).

In the text that follows, these plasma types will be referred to respectively as **Recovered FFP and Source FFP.**

Plasma collected from selected donors having antibodies of special therapeutic efficacy is described as SPECIFIC PLASMA - it may be collected as either Recovered or Source FFP.

OUTDATED PLASMA is recovered from whole blood which has exceeded its 35-day shelf life.

Uses of plasma

All plasma-derivatives may be manufactured from FFP or SPH.

Outdated plasma can be used to manufacture albumin and immunoglobulin.

Specific plasma is used to prepare specific immunoglobulins such as anti-tetanus.

Distribution of plasma types

Plasma **recovered** from blood or platelets is invariably **collected** by state/non-profit blood transfusion services using the panels of voluntary unremunerated blood donors. These same donors are now increasingly donating plasma by apheresis where volume targets are not recovered from whole blood.

Blood and platelet donors in Europe and USA are invariably voluntary and unpaid and National or Red Cross Blood Transfusion Services inevitably provide most plasma as **Recovered.**

The commercial sector, predominantly represented in the USA, relies mainly on paid-donor SPH collected either at their own apheresis centres or from commercial SPH procurement agencies. The commercial sector may also contract to purchase some unremunerated donor Recovered plasma when demand dictates.

Plasma, mainly Recovered, is sold by brokers or agencies, on a spot-market basis.
All USA plasma must be FDA certificated for use or export with the exception of outdated plasma for which no export certification is required.

Plasma brokers are also able to supply intermediate products of plasma fractionation either on contract or at spot-market rates. Such intermediates are controlled by specification as set out in the manufacturer's relevant product registration files.

Commercial fractionators directly control their plasma supply to minimise the high cost of plasma inventory. The paid-donor apheresis programme is flexible and rapidly responsive to changes in plasma demand through the collection schedule. Supply of Recovered plasma from whole blood is controlled by the demand for blood NOT by the demand for plasma by the state/public sector fractionator. Frozen plasma inventories frequently exceed fractionation demand and represent costly unplanned overheads on the Blood Services. Frozen Plasma is stable for many months at temperatures below -30°C: BPL plasma inventory exceeds six months' supply at present.

PLASMA SUPPLY AND DEMAND: INTERACTIONS

There have been major changes in market demand for plasma products both in terms of total market volume and individual products, and these changes have had a significant impact on plasma demand and specification.

Until 1986 the worldwide industrial fractionation and source plasma programmes were driven by albumin demand. However, in the mid-80s the industry in both commercial and state sectors had to resolve the crisis which AIDS had caused and which led to the following sequentials:

Event	Effect
An acute reduction in blood availability and demand	A short-term increase in demand for albumin (safe) and source plasma
An immediate requirement for a virus-safe factor VIII of higher purity	An acute drop in process yield and corresponding increase in demand for plasma
Japanese worries on imported HIV-positive products accelerates self-sufficiency programme	Sharp drop in volume for USA plasma product exports to Japan - particularly albumin.

By 1987, the worldwide plasma fractionation programme was driven by Factor VIII demand. Factor VIII price increased abruptly by up to 350% in the USA. At the same time, the readjustment in industrial planning had to consider the future effect of recombinant Factor VIII on the plasma market.

By 1990, process yields of main products per kg of plasma processed had been restored to pre-1985 levels i.e.

Albumin	25 g/kg
Factor VIII	**200 iu/kg**
Immunoglobulin	2.5 g/kg
Factor IX	200 iu/kg

Fluctuations in product demand, particularly factor VIII, have been resolved in the short term by changes in plasma supply and fractionation capacity but not by further improvement in factor VIII yield (Baxter's Hyland Division have sold off all their licensed paid-donor apheresis centres). Accordingly, if main product markets are

Albumin	250 kg
Factor VIII	3×10^6 iu
Immunoglobulin	10 kg
Factor IX	$.6 \times 10^6$ iu

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and plasma collection for fractionation is at 10,000 kg (10 tonnes), net manufacturing outputs are

Albumin	250 kg
Factor VIII	2×10^6
Immunoglobulin	25 kg
Factor IX	2×10^6 iu.

(all figures are per million population)

At the above level of plasma supply, all but factor VIII demand is met with capacity for immunoglobulin and factor IX well in excess of current estimates of market size.

To increase plasma procurement for factor VIII production is to distort further the economic imbalance between plasma supply and product demand unless factor VIII can accommodate the full incremental plasma oncost.

Factor VIII demand continues to increase. In the UK, use of factor VIII will probably reach 150×10^6 iu during this decade but questions of considerable importance for the industry remain unanswered:

- In the UK and Europe 50% of haemophiliacs under treatment are HIV positive. Will the deaths from AIDS be balanced by newly diagnosed haemophiliac infants? What will the size of the treatment group be in 10 years' time?

- Will recombinant factor VIII provide a satisfactory alternative treatment and how soon will the product be readily available for routine prescription?

- Will recombinant factor replace plasma factor VIII? When and why?

Factor VIII from plasma has become the industry's lead product **only slightly ahead of a potential major change in market preference.** The effect on plasma demand and fractionation is far reaching and self-evident.

DISTRIBUTION

Plasma fractionation is distributed between public and private sectors in USA, Europe and Japan.

In USA, with a capacity of $\sim 6 \times 10^6$ litres p.a., commercial fractionation takes precedence (American Red Cross are in contract fractionation with Baxter Healthcare at their Hyland Division - volume $\sim 1.2 \times 10^6$ litres p.a.).

In Japan, the Red Cross have progressed a self-sufficiency programme while Green Cross and their USA affiliate Alpha remain the commercial arm.

In Europe, plasma-derived products account for a plasma demand of some 7×10^6 kg p.a. of which, capacity in the state/public sector provides 50%. Commercial industrial interests are present in Austria, Italy, Scandinavia and Germany. Austria and Italy have joint capacity for plasma of some 2.5×10^6 kg p.a. of which an estimated 70% is sourced by USA-derived paid donor plasma or USA certificated recovered plasma (available through brokers).
State (non-profit) plasma fractionation facilities in Europe are present in UK, France, Switzerland, Holland, Finland and Belgium. Their purpose is to receive plasma recovered from whole blood and apheresis plasma provided by the national unpaid voluntary-donor transfusion services.

In Europe, state fractionation services are plasma-sourced to some 3.5 million kg p.a. equivalent to 10 tonnes/million population i.e. sufficient plasma to meet all plasma derivative markets except factor VIII.

The plasma requirements of BPL

BPL has a current working capacity of 500 tonnes FFP which it is believed could be extended to 750 tonnes by appropriate changes to some equipment capacities and to working practices.

The Blood Transfusion Service is able to supply Recovered FFP from whole blood at an annual rate of ~425 tonnes, leaving ~75 tonnes to be augmented by SPH from apheresis to reach the target of 500 tonnes. **Any increase** in supply of plasma to BPL from NBTS **over 500 tonnes p.a. must** be found by apheresis SPH or recovered from platelets collected by automated cell separator procedures.

Recovered FFP is the most economic category of plasma supplied to BPL. As explained, 500 tonnes FFP will source the **needs for all products except factor VIII:** 722 tonnes is needed to meet current NHS demand for 130 million iu factor VIII at 180 iu/kg FFP (or 650 tonnes at 200 iu/kg FFP yields).

All plasma over 500 tonnes p.a. processed by BPL will increase the excess of products (other than factor VIII) above NHS market requirements and these excesses need to be sold outside the UK.

Traditionally BPL has been mandated to manufacture only from NBTS voluntary donor plasma, but a recent approval has been given to manufacture on contract from voluntary unpaid donor plasma on the understanding that the products are returned to the contracting organisation for sale outside the UK.

BPL PLASMA OPTIONS

BPL can adopt various strategies on which to base operational planning, e.g.:

Option 1	Effect
Limit operations to processing NBTS plasma based on current targets > 560 tonnes p.a.	- Factor VIII output > 110M iu p.a. - Albumin self-sufficiency - IgG, Factor IX, NHS excess - Retains under-use of plant capacity - Requires continued import of commercial factor VIII
Option 2	
Extend operations to 750 tonnes p.a. based on increased NBTS plasma supply	- Factor VIII output -> 150M iu p.a. - Albumin, IgG, Factor IX, NHS excess - Full process plant occcupancy - Requires purchase of >300 tonnes of premium SPH p.a.
Option 3	
Extend operations to 750 tonnes p.a. 500 tonnes NBTS plasma + 250 tonnes imported recovered plasma All products available to NHS	- NHS product demands met - Albumin, IgG, Factor IX, NHS excess - Full process plant occupancy - Imported plasma at commercial contract prices

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Option 4

Extend operations to 750 tonnes p.a. 500 tonnes NBTS plasma products distributed to NHS 250 tonnes contract toll manufacture products -> plasma supplier	- Factor VIII below NHS demand - Commercial Factor VIII import needed - Full process plant occupancy - Economic benefits of toll manufacture - Limited BPL commitment to sell products excess to NHS demand

Option 5

Fractionate 500 tonnes NBTS plasma p.a. Process imported cryoprecipitate to meet NHS Factor VIII demand ? Some toll manufacture of plasma	- Meets all NHS product demands - Minimises excess products from NBTS plasma - Minimises investment in plasma programme expansion - Full process plant occupancy - Limits plasma expenditure for BPL

Comments

- At present only Options 1 and 4 are authorised with the caveat that toll manufacture would involve only plasma from **unpaid voluntary donors.**

- Under Options 1 and 4, regardless of preference, the NHS is compelled to buy imported factor VIII products, even though these are prepared mainly from **paid** donor plasma.

- The paid donor plasma element in imported commercial factor VIII products does not, however, prevent grant of a UK Product Licence by the Medicines Control Agency.

- BPL cannot currently have access to paid donor plasma or the intermediate products of that plasma.

- Option 2 probably represents the most expensive plasma route to full BPL capacity and NHS Factor VIII self-sufficiency. NBTS will require capitalisation to achieve this growth in SPH output and the expanded plasma demand for factor VIII may be shortlived if recombinant factor VIII meets market expectations and/or if the haemophilia population contracts from AIDS deaths. BPL would have a major task in exporting the incremental product excesses of albumin, IgG and factor IX.

- Option 3 is a cheaper and more flexible route to provide NHS self-sufficiency and the economic benefits of full BPL process plant occupancy. BPL retains control of plasma inventory **above** the NBTS rate of 500 tonnes p.a. BPL can import certificated recovered FFP from unpaid voluntary blood donor sources. NBTS capitalisation in plasma procurement is avoided.

- Option 4 provides BPL with economies of scale-up and contract revenues without the responsibility for distribution for products from the plasma incremental to NBTS supply.

NHS must continue to buy factor VIII but this demand may be met eventually by recombinant product.

- Option 5 sources BPL capacity and NHS product demand in the most controlled, flexible and economic way. It provides a means of retaining full process plant occupancy while minimising the need to sell excess intermediates and finished products.

General

In the event that recombinant factor VIII displaces plasma factor VIII below the level of 2M iu/million population, then either albumin or intravenous IgG will return to drive plasma demand by the industry.

For BPL, the current level of NBTS plasma supply is close to that needed to supply albumin to meet full NHS demand. The present, possibly short-term, plasma factor VIII demand by NHS is logically better resolved by the use of imported plasma or cryoprecipitate to augment NBTS plasma supply than to promote a speculative expansion of the national apheresis programme.

BPL is not authorised at present to import plasma or cryoprecipitate to make products for sale to NHS.

PLASMA PRICES

Plasma collected by commercial fractionators (Source FFP) carries the lowest value added costs to the fractionation process: this includes negotiated contract supplies between the commercial fractionator and the commercial apheresis agency. Prices for this plasma are not publicly quoted.

There is a spot market for plasma which reflects significant variations in plasma demand even within relatively short time intervals. The spot market quotes for Source FFP, Recovered FFP and Outdated Plasma.

A high percentage of plasma for sale on the spot market is Recovered FFP collected by national institutions such as the American Association of Blood Banks affiliates. A current set of spot market rates/kg are provided below:

Source FFP	$65
Recovered FFP	$55
Outdated Plasma	$50 (reflecting current acute albumin shortage post Gulf war)

It is believed that the value added of commercially collected plasma to the industrial process is significantly below spot market rates.

Currently determined prices for plasma/kg in the UK are

Source FFP	£60 ($102)
Recovered FFP	£35.80 ($61)

Prices for specific antibody plasma vary according to the type and potency but has no immediate relevance to spot market rates for plasmas quoted above.

It should be noted that anticoagulant water in recovered plasma/kg is higher than in commercial source plasma - thus protein content/kg plasma is lower in recovered FFP, and is reflected in reduced product yields.

R. S. LANE,
10 May 1991.

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