MEMO

PRIVATE & CONFIDENTIAL

To: Colin Walker
Pim van Aken
Dennis Allison
Lawrence Banks
Jennie Gubbins
Keith Peters
Angela Robinson
Barry Savery

From: John Adey

Date: 16 January 1998

Subject: **BPL**

This is what I am proposing to send to the Department. Please can we discuss on Tuesday.

GRO-C: John

John F Adey
Chief Executive

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DRAFT
20 January 1998

Dr Graham Winyard
Director of Health Services
NHS Executive
Quarry House
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Dear Graham,

Further to our meeting on 19 December and your subsequent letter dated 31 December I enclose as promised a paper detailing our thoughts on the options for BPL.

We recommend a course of action - the limited purchase of unpaid donor plasma, specifically cryoprecipitate to make Factor VIII, from the USA by BPL which, in our view, provides the opportunity to maintain something like a steady state at BPL (and in the NHS) until more information is available about *nv*CJD transmission. It avoids the need for more precipitate general decisions and also will allow time for a better informed assessment of the longer term financial impact. I acknowledge, however, that the situation, when viewed from a perspective other than the NBA's might mean that other options are considered more appropriate.

The paper makes the point that a decision is needed soon so that BPL can enter the contracting round in February with a clear message for its customers and consequently I would be grateful if this could be dealt with as a matter or urgency.

Please let me know if you need anything else.

Yours sincerely,

John Adey

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Chief Executive

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BPL
Bio Products Laboratory

BPL and the Impact of new variant CJD

PURPOSE OF PAPER

The recall of several batches of BPL product due to their having been manufactured from plasma from donors who subsequently died from new variant CJD (nv-CJD) has potentially very damaging consequences for BPL in the immediate future. This paper sets out the possible options open to BPL in the short term and their likely costs and consequences and recommends a way forward.

The paper assumes that Ministers judge the risk from nv-CJD associated with blood products to be sufficiently low that BPL should continue to offer products manufactured from UK source plasma. If nevertheless the risk is judged large enough that Ministers feel it would be appropriate to reduce risk by funding fully recombinant Factor VIII for haemophiliacs then the knock-on effect of that would almost inevitably lead to closure.

RECOMMENDATION

BPL should be permitted to purchase limited quantities of US origin unpaid donor raw material, specifically cryoprecipitate to make Factor VIII, to supplement UK plasma and to meet the needs of those clinicians and patients who are at present not prepared to use UK source material. The intention is to buy time at low cost to preserve BPL as a viable operating entity while awaiting further information on the risks of nv-CJD and exploring options for the longer term future of the BPL business while minimising the total revenue cost of the BPL operation.

An early decision is important to avoid a rapid decline in BPL's business and to permit BPL to make the necessary arrangements to offer product options to its customers in time for the new contract season.

If BPL is not permitted to purchase US raw material, it will be necessary for them to offer some key employees a loyalty bonus to retain their services, otherwise BPL may be forced into premature closure with a resulting shortage of product for UK patients.

BACKGROUND

Annexe A gives details on:-

- What is BPL?
- Funding History

Historically, plasma sourced from UK unpaid blood donors has been considered one of the safest sources of blood products in the world. The experience of HIV in the early '80's confirmed the higher level of risk particularly associated with US paid donors of plasma.

However, the emergence of nv-CJD in the UK has brought into question the whole safety of the UK blood and plasma supply as the UK is currently the only country perceived to be at risk from nv-CJD.

BPL instigated two recalls of plasma products in October/November 1997 as they had been made from blood donations from donors who subsequently died of nv-CJD. This was a particular concern to the haemophilia treaters who were already lobbying hard for sufficient additional funds to purchase recombinant Factor VIII as that product was perceived to have a lower viral risk even though it contained a blood product, albumin, as a stabiliser. The haemophilia treaters, through their central UK organisation, made public in The Lancet their intention to press further for full central funding of recombinant Factor VIII and if that was not available they recommended the use of products sourced from nv-CJD free countries, primarily the USA.

Since that time some haemophilia treaters have implemented that decision and switched from BPL to US-sourced material. Others have decided to remain with BPL product and a third group are following the wishes of their patients. The patients in turn are either strongly pro or anti BPL UK product or are unconcerned as to the source.

Overall there is a clear preference for US-sourced product which would become a very strong conviction if a further recall became necessary.

The other key group of clinicians and patients is the immunologists and their dependent group of primary immune deficient patients. This group has largely taken the view that supply of adequate quantities of product in a high growth market is a higher priority than concern over risks of transmission of nv-CJD and there are likely to be limited moves by this group away from BPL product. The users of the third main product, albumin, are very diverse and concerns over nv-CJD are limited although some hospitals have already confirmed an intention to move away from UK-sourced products.

A number of users hold the view that the nv-CJD issue is a relatively short term one. Tests to identify and eliminate suspect donations and a means of eliminating infectious particles from BPL's manufacturing processes are expected over the next year or so and there is as yet no evidence of an nv-CJD epidemic to increase concern. Hence, many of BPL's customers would not wish to lose the possibility of purchasing from a UK manufacturer with all the security that provides, particularly if it were a reaction to a relatively short term problem.

MARKET PROJECTIONS

Any projections at present inevitably suffer from a high level of uncertainty. Initial very strong reactions by some customers have been tempered over time and BPL sales in December remained reasonably strong in both domestic and export markets.

However, BPL has a very large position in the UK market and a substitution of such large quantities of product very quickly would not be feasible. It takes time to fill, pack and label appropriate material and get every batch released by NIBSC prior to shipment. In addition, recombinant Factor VIII availability has been relatively tight. Hence, although BPL expected and has seen some short term reduction in sales (£2m/yr exports and £3m/yr in UK) they were not expecting any major reduction before February or March. However, a significant change could occur in April at the start of the new financial year. Annual contracts for BPL products are not negotiated until February or March and hence no precise predictions of customer intentions can be made now but that in turn points to the need to have an early and very clear message to customers on what products can be offered before contracts are agreed.

Export predictions are equally difficult. Some European markets are extremely concerned about nv-CJD in UK products. France and Portugal have already banned imports from the UK and both Germany and Austria would certainly take a similar line if BPL was to offer products there. The recall of Amersham products containing BPL albumin has publicized very widely across the world the potential risk from UK blood products but BPL's major export markets which are mainly in the developing countries have so far continued to order products. If there are no further recalls and the real risk of nv-CJD transmission continues to be perceived as low, then they would hope the impact on their business would be limited over and above those European contracts already lost. BPL had forecast very substantial growth in export markets but those forecasts now look extremely optimistic particularly for 1998/99.

In the light of all the above, a number of scenarios have been considered and costed which broadly cover the likely range of options. These are shown in summary on the chart in Annexe B and in detail in Annexe D. Annexe E gives a summary of the latest view of 1997/98 results compared with the longer term forecasts and the most recent PES bid. The scenarios are summarised below:-

Scenario 1 - Base Case

This is an unlikely scenario as it assumes haemophilia directors will not move to US-sourced products but a significant increase in purchases of recombinant Factor VIII had been included in previous forecasts.

UK Factor VIII sales are estimated to be in line with the PES bid for 1998/99. This is a substantial reduction on actual 1997/98 sales.

UK Albumin and Immunoglobulin sales are estimated to be 10% less than PES bid as it is inevitable some purchasers will prefer imported product.

Exports are reduced by 20% as PES assumptions were optimistic and some markets are already closed to BPL.

The overall effect in 1998/99 is to increase the revenue funding requirement from £10.7m to £16m.

The position in 1999/2000 is impossible to predict at present as it will depend on nv-CJD developments and whether or not further recalls are made.

Scenario 2

This scenario is split between two options depending on whether or not BPL sources some US raw material.

a) BPL only offers UK plasma derived products.

In this case BPL believes there will be a rapid and substantial move towards imported products. Haemophilia treaters have been assured by importers that adequate supplies of both recombinant and US plasma derived products will be available to them. Importers will put very strong pressure on purchasers of all products as they will see an opportunity to force BPL out of the market.

BPL employees will see an inevitable decline in BPL's future prospects and the best people will start to leave. If key employees cannot be retained BPL will not be able to continue to comply with pharmaceutical regulations and would have to cease manufacture. This in turn could lead to serious interruptions in product supplies to hospitals in 1998 as importers adjust to very large increases in demand.

BPL estimates a net funding requirement in 1998/99 of £23m-£27m and the DOH will also have to cover additional costs of higher priced imported products, particularly recombinant Factor VIII, estimated at between £10m and £15m.

b) BPL imports some US raw material in addition to using UK plasma.

This assumes BPL imports cryoprecipitate from American Red Cross to make Factor VIII so that haemophilia treaters have a choice of product. They would continue to offer a full range of products made from UK plasma.

Such a move would substantially deter importers who would see it as much more difficult to force BPL out of business. However, some UK and export sales would inevitably be lost but the effect is estimated as similar to scenario 1.

The additional raw material cost is estimated at £2m but not all of that need be committed initially.

Total revenue funding requirement is estimated at £18m in 1998/99 cf PES £10.7m.

This option preserves BPL's market position until more information is known about nv-CJD transmission.

Scenario 3

Recombinant Factor VIII is "fully funded".

This assumes BPL continues to offer products sourced from UK plasma only but DOH decides to fund the full cost of recombinant Factor VIII for all haemophilia treaters. A substantial loss of business will occur through 1998/99 similar to scenario 2a with a similar impact on staff and BPL's ability to continue to manufacture.

BPL funding requirement for 1998/99 estimated at £25m and the additional funding by DOH for recombinant Factor VIII is estimated at £24m in 1998/99 as it is assumed extra supplies of recombinant product will become available at an increasing level through the year. Extra full year cost would be £35m (£30m excl.VAT).

Scenario 4

UK plasma is unacceptable as a raw material.

BPL could continue to function based on purchased US plasma and cryoprecipitate. The current PES funding of £10.7m would be adequate but there would be a shortfall in NBA funding for blood centres of £23m and 600T p.a. of plasma would have to be destroyed.

CONCLUSION

The possibility of transmission of nv-CJD in blood and blood products has already affected BPL's sales and unless urgent action is taken, BPL could be forced to cease manufacture. A pre-emptive move to import US-sourced Factor VIII raw material from unpaid donors to offer UK haemophilia treaters a choice of product is believed to offer a good chance of limiting the impact of nv-CJD on BPL in the short term. However, unless BPL is able to advise customers of their intentions by early February, it may be too late to implement such a change before too much of the market commits to imported product.

FUTURE OF BPL

If BPL is not permitted to purchase US raw material then closure seems inevitable.

Redundancy costs and clean up are likely to be approximately £15m with only around £3m offset from realisation of net current assets.

The value of the Elstree site is difficult to estimate but is probably of the order of £5-£20m.

BPL has potential for further development almost certainly in some form of alliance with another manufacturer which would then remove any future funding requirements from the DOH.

This issue has received much consideration over the last six years and more. The NBA Board proposed a formal partnership with a major manufacturer, Bayer, in 1995 but this was rejected by Conservative Ministers. Prior to the advent of nv-CJD BPL developed a much stronger position than when the partnership was proposed and many changes have also occurred across the world of fractionation which means that possible options for BPL's future have changed but still remain.

BPL is forecast to require continued financial support in the longer term if it remains an independent unit within the NBA as it is not large enough to fund its essential future development from its own earnings (see Annexe E). This is the case for most

of the world's fractionators other than the largest international companies and even there, there has been substantial consolidation. A reasonably viable manufacturer now needs to be fractionating around 1000T p.a. of plasma, compared with BPL's 600T p.a., and needs a wide product range and a substantial product development portfolio. The major world manufacturers, Baxter/Immuno, Centeon and Bayer, all fractionate over 2000 tonnes per year and offer a wide range of products.

Substantial rationalisation will take place over the next few years both within the commercial and not-for-profit sectors and there are undoubtedly opportunities to secure BPL's longer term future by some form of partnership. However, in view of the past history, potential partners have made it clear that they would not be prepared to explore any arrangements in detail unless the principle of partnership has the full support of Government Ministers from the outset. The financial logic of a partnership is impeccable and the NBA Board is fully convinced that such a move would not have an affect on donors and hence the collectibility of whole blood. The Board would therefore propose, subject to BPL continuing to manufacture, putting a paper to Ministers setting out the case for BPL partnership and broad potential options as pre-cursor to entering discussions with potential partners.

ANNEXE A

BACKGROUND

What is BPL?

1. BPL, which is managed by the National Blood Authority and located near Elstree, Hertfordshire, was set up in order to meet the Government commitment to self sufficiency in blood products, in particular in coagulation factors - primarily Factor VIII - from voluntary unpaid donors in England and Wales. BPL has for some years been able to meet the clinical demand for its products. (Clinicians have been free to purchase products from other suppliers). It employees 480 staff with an annual turnover of around £55 million.

2. After blood has been collected, most of it is split into three parts - red cells, platelets and plasma. The amount of blood collected is driven by the clinical demand for red cells. BPL takes all the plasma collected in England and Wales (apart from small quantities for clinical use) - about 600 tonnes - and fractionates it to produce coagulation factors (notably Factor VIII for haemophilia), albumin and immunoglobulins. BPL has spare capacity and could fractionate about 750 tonnes of plasma at present, which could rise to 1000 tonnes with some limited further capital investment.

3. BPL pays blood centres for the plasma and sells its products to NHS and independent hospitals in England and Wales. It also exports surpluses where it can. BPL does not currently turn all it's plasma into the full range of products as it has only in the last 2 years had a licensed intravenous immunoglobulin, a high growth product. This severely affects BPL's financial performance. A successful fractionator makes and sells as many products as possible.

4. NHS hospitals are not bound to buy BPL's products. There are alternative commercial suppliers of plasma-based products, which use plasma from paid donors in the USA and elsewhere. Prices in the UK are low by international standards - the NBA believes strongly that this is as a result of BPL's presence in the market, though the arrangements for setting prices in different European countries vary - and some commercial companies will not supply the UK market for this reason. There is, however, one aggressive competitor (Alpha) which is determined to more or less match BPL's prices on coagulation factors. More recently, recombinant coagulation factors have come onto the market. The effect of this is considered later.

5. Scotland has its own Plasma Fractionation Centre (PFC), which also fractionates plasma from Northern Ireland. It fractionates about 84 tonnes of plasma a year. The PFC forms part of the Scottish National Blood Transfusion Service, and the PFC neither pays for the plasma it fractionates, nor charges for the products it supplies to NHS hospitals in Scotland. It does, however, charge non-NHS customers and sells some products to the NHS in England and Wales, in competition with BPL.

6. Over the years there have been substantial changes.

- Originally there was shortage of plasma, which led the Blood Transfusion Service (BTS) to develop plasmapheresis (removing plasma from the blood and returning the rest of the blood to the donor). There is now in general more than enough plasma to make the volume of product which BPL is able to sell in a free market (although BPL has been short of plasma in 1997).

- Between 1986/87 and 1996/97 the clinical demand in England and Wales for Factor VIII (which represents over 50% by value of all BPL's ales) grew from 80 million iu (international units) to about 150 million iu. In 1995-96, BPL took more than 70% of the market for plasma-derived Factor VIII and this share rose to around 80% in 1997 before the recalls due to nv-CJD. However, the entry of recombinant product into the market, albeit more slowly than BPL anticipated, means that its overall market share is now 60%-70%. As use of recombinant product grows, BPL will be severely affected.

- The price of plasma-derived Factor VIII has fallen from 39p/iu to 25p/iu in 6 years. (Recombinant Factor VIII costs a little over 50p/iu incl. VAT, though some very big purchasers may be able to buy it at 47p/iu).

- Use of albumin in the UK has historically been lower in other countries, but some other countries are now reducing their usage. Albumin is BPL's main export product.

- BPL are now able to produce an intravenous immunoglobulin (Vigam S and Vigam Liquid). This is an expanding market, with an increasing number of indications for use of IVIG.

- The private sector has paid for blood and blood products since 1984 on the basis of cost-recovery. DH determined levels. Cross charging for blood products in the NHS was introduced in April 1989. The level of reimbursement to blood centres for plasma was set by DH and the cost of products charges to hospitals was determined by bulk negotiation. In April 1991 charging was extended to blood as part of the "Working for Patients" White Paper philosophy. Since 1994 the prices of plasma and the resultant blood products have been under the control of the NBA.

Funding History

7. BPL exists to make the best use of the blood donor's gift, and to secure self-sufficiency, not to make money. However, with the introduction of charges to the NHS for BPL products in 1989/90, BPL has been operating on a commercial basis. The following table shows that DH has nonetheless had to subsidise BPL in all but one of the years since it was founded, as well as putting in capital investment. Of course, if BPL had not existed, and capital investment had not been made, expenditure would have been incurred to obtain the products which BPL makes. This might or might not have been greater than the sums set out below, plus the cost to the NHS of buying the sort of products which BPL makes, whether from BPL or its competitors. It is impossible to know.

BIO PRODUCTS LABORATORY - DH FUNDING

	Revenue £000	Capital £000	Total £000
1984/85	4,535	17,000	21,535
1985/86	3,268	13,915	17,183
1986/87	6,807	14,818	21,625
1987/88	8,864	8,056	16,920
1988/89	10,444	4,089	14,533
1989/90	12,885	7,924	20,809
1990/91[1]	13,524	3,640	17,164
1991/92[2]	13,002	3,428	16,430
1992/93	1,629	947	2,576
1993/94	5,765	2,744	8,509
1994/95	(806)	2,164	1,358
1995/96	5,231[3]	2,000	7,231
1996/97	7,627	2,350	9,977
1997/98	9,451[4]	4,500	13,951

[1] This was the last year in which BPL products were supplied free of charge to the NHS.

[2] BPL received transitional funding to purchase stocks of plasma and for setting up charging systems.

[3] Capital charges of £4.4 million were levied for the first time on BPL's revenue account.

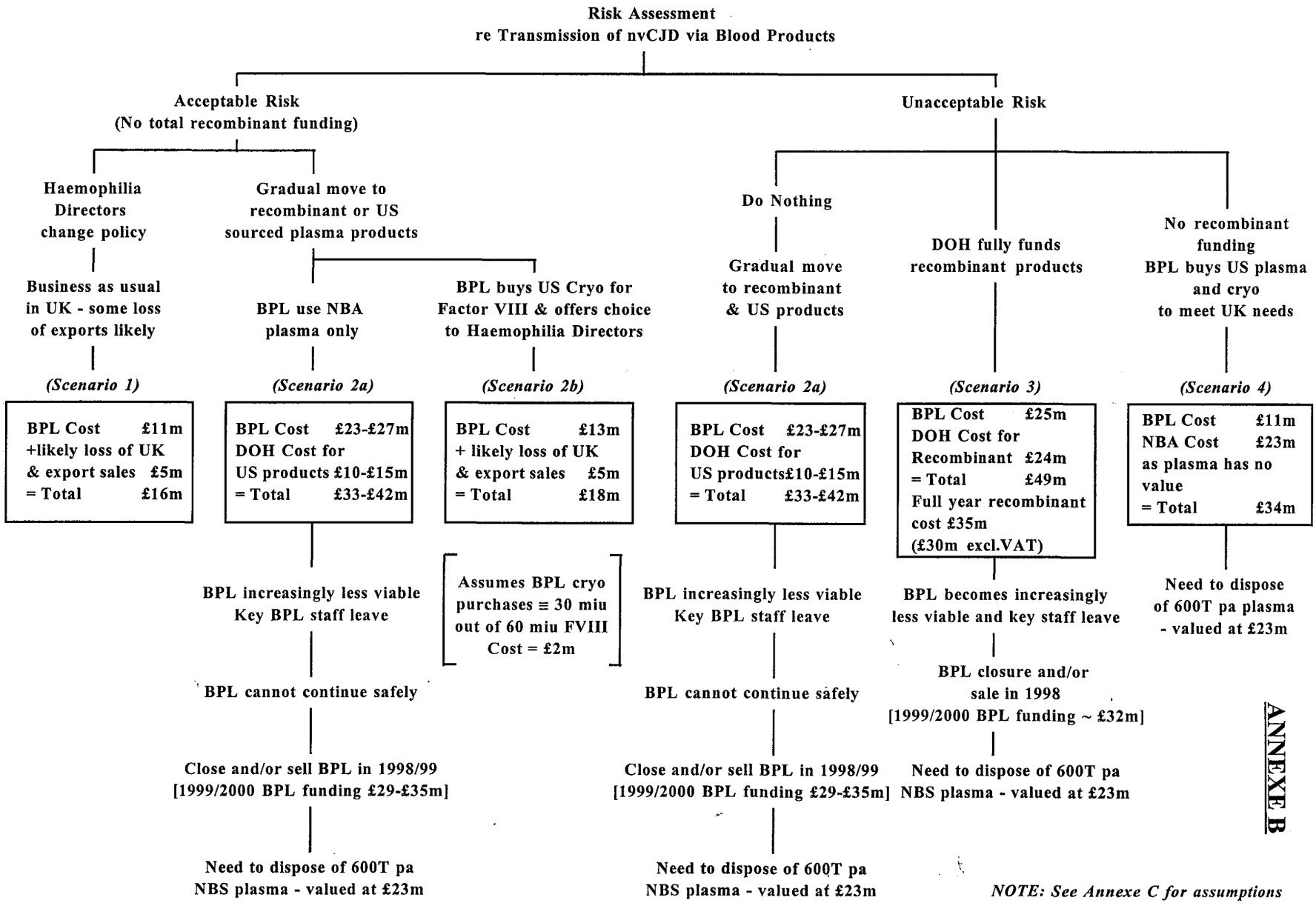
[4] Capital charges were increased to £8.2m due to a revised basis of charging.

8. It can, of course, be argued with some justification that this presentation of the facts is unfair to BPL. They take all blood centre plasma at a fixed price. They might improve their financial performance if they took in less plasma, or paid the price for it which a commercial fractionator would be prepared to pay, given that they had to buy all of the blood centre plasma. That would transfer the problems to the blood centres, and the NBA would have to raise the price which hospitals pay for red cells, etc. But this would still leave a need for the longer term future of BPL to be addressed.

9. The constraints of public funding , and the rules governing "not-for-profit" organisations make it difficult for any publicly funded organisation, however, efficient, to operate effectively in the market. Such organisations find it particularly

difficult to compete with commercial competitors which are structured and financed flexibly in order to meet the requirements of the market in which they operate. There are also considerable problems over investing in new technology.

1998/1999 Scenario



ANNEXE B

NOTE: See Annexe C for assumptions

ANNEXE C

Assumptions

1. **PES Bid £10.7m Revenue funding**

   FVIII 50-60 miu (70% of plasma market)

   Vigam 30% share of fast growing market

	£m	
UK Coag sales	17.9	
UK Albumin	13.1	
UK Immunoglobulin	9.1	
Exports	13.4	(9.5 Albumin, 2.5 CF, 1.4 Vigam)
Total Sales	53.5	

2. **All scenarios vary manufacturing/QC costs and stocks.**
   Overheads are fixed but exclude IT Project and MAD expenditure.
   No inflation, 600T pa plasma ex NBS, no ALT testing of donations.

3. **If only use UK plasma - compared with PES bid:**

   FVIII declines 30% ⇨ 50% or 50% ⇨ 80%
   Albumin declines 10% ⇨ 30% or 20% ⇨ 40%
   Vigam declines 20% ⇨ 30% or 40% ⇨ 50%
   Exports decline 50% (40% 1st half, 60% 2nd half)

   Anti-D ⇨ 30%
   No tetanus or normal intramuscular IgG

4. **If purchase cryoprecipitate from USA:**

FVIII	as for PES bid
UK Albumin	PES bid less 10%
UK Vigam	PES bid less 10%
Exports	PES bid less 35%

5. **If recombinant FVIII fully funded:**

   Recombinant supplies increased evenly over four quarters of 1998/99 to reach 90% of total market.
   BPL FVIII assumed to have 50% of remaining plasma derived market.
   Albumin reduced by 20% (from PES bid).
   Vigam: 1998/99 expected outcome less 10%.
   Exports 50% of PES bid.

ANNEXE D

Scenario 1 - Base Case

This is the base scenario against which other options are measured and in all cases it is assumed BPL purchases all NBS and NBTS Wales plasma at current prices.

In the unlikely event that the Haemophilia Directors remove their recommendations to use recombinant or US plasma derived Factor VIII, or perhaps more likely simply ignore those recommendations, then BPL would expect UK Factor VIII sales to be close to those in the 1998/99 PES bid at around 55-60 i.u. This would be a substantial reduction compared with the very high levels achieved in the current year, but is considered realistic in the light of all the current circumstances.

Albumin sales will be around 10% less than in the PES bid as the trend to cheaper alternatives continues and some product will be lost to competitors.

Immunoglobulin forecasts assumed substantial growth and the recent launch of Vigam Liquid will help but the PES assumptions now look optimistic and a shortfall of 10% seems likely.

So overall domestic sales will fall short of PES assumptions. On exports it had been assumed that all albumin surplus would be sold overseas and that there would be substantial Vigam and Factor VIII exports. This now looks very optimistic and a significant shortfall on all products is now expected. Total exports of £8.7m, compared with the forecast of £13.4m (and likely 1997/98 sales of £9.5m) are the highest that might be expected but the confidence limits are quite wide. Hence total 1998/99 sales are likely to be £6.5m lower than the PES forecast which would lead to a revenue funding increase from £10.7m to £16m.

It is extremely difficult to forecast the forward position from April 1999 onwards as it is highly dependent on developments with nv-CJD, perceptions of risk and whether or not BPL had made further recalls in the previous year. No further product recalls but a continuing uncertainty over nv-CJD risk would be likely to lead to the business languishing at the level reached in April 1999 with on-going revenue funding at around the same level. Further recalls would be likely to push the business into a very difficult position but the alternative of a removal of uncertainty would free the business from market constraints and give the opportunity to start developing export business again. So revenue funding requirements would reduce but not substantially as ground would have been lost against competitors.

Scenario 2

This assumes that the risk associated with nv-CJD is "acceptable". There is no decision to fund recombinant for all but haemophilia directors are continuing to seek US-sourced plasma Factor VIII. This scenario is split between two options depending on whether or not BPL sources some US raw material.

(a) BPL only offers UK plasma derived products.

This will be seen by customers as an inflexible "head in the sand" attitude refusing to recognise customer concerns. It will encourage competitors who will see a real opportunity to force BPL out of the plasma products market. They will therefore make enough product available at favourable prices to attack and capture a substantial market share of all products over the next 12 months.

In addition, competitors would put particular pressure on BPL's export markets and a substantial decline is forecast there. The overall impact is a net funding requirement in 1998/99 of £23m to £27m. If BPL was able to continue manufacturing in the year 1999/2000, the funding requirement would be in the range £29m to £35m.

This very major and continuing reduction in sales could well lead to BPL being unable to function satisfactorily even during 1998/99 as key staff would leave and it would not be possible to remain in compliance with its pharmaceutical licensing requirements. Loyalty payments to retain key staff could certainly slow this process down but of course are "ultra vires" without specific Ministerial approval.

BPL would only be fractionating between 340 tonnes and 370 tonnes of plasma during 1998/99 compared with a supply of 600 tonnes and hence stocks would build to the point where BPL was unable to store any more plasma on site. Thereafter it would be necessary to destroy or seek external storage but with an on-going demand of less than half the supply of plasma, the only logical course would be to destroy any surplus.

In addition to BPL revenue funding there will be additional costs of higher priced imported products, particularly recombinant Factor VIII. These are estimated to range between £10m and £15m in the year.

(b) BPL imports some US raw materials in addition to using UK plasma.

This assumes BPL continues to offer UK plasma derived product, thus demonstrating confidence in them but in addition is willing to offer products made from US plasma or intermediates where customers insist on it. BPL has identified a source of unpaid donor raw material from the American Red Cross which would be sufficient to meet their needs at prices similar to that BPL currently pays.

The demand for US-sourced material is expected to be mainly from the haemophilia treaters and sufficient Factor VIII intermediate can be purchased at a reasonable price to meet that need. No more than half the demand is expected to be for US material and the additional cost to the business would be a maximum of £2m in the full year although of course it would not be necessary to commit immediately to that full sum and an initial commitment of less than £1m to meet the first six months requirement would be adequate to evaluate the impact.

BPL believes it can demonstrate adequate cleaning of the manufacturing facility and where this may be difficult, for instance in chromatography columns, parallel systems can be installed to ensure adequate raw material separation. BPL recognises the need to satisfy the MCA of the validity of its cleaning procedures. Assuming co-operation

from the MCA and NIBSC with whom discussions have already been held, BPL could be delivering fully licensed product from US raw materials by mid-year and if they were able to advise customers early enough of that intent they believe they could persuade them not to move their business to competitors. In addition, there is the possibility of purchasing finished Factor VIII from the American Red Cross for re-sale to UK haemophilia treaters as an interim measure even though this would be on a named patient basis. As Ministers are aware, this has already been raised publicly by one haemophilia treater who has requested BPL to act in just this way.

The affect of all the above would be to preserve BPL's market position while awaiting further developments on nv-CJD. Competitors would realise the costs and risk of a major attack on BPL's business would be unlikely to succeed so they would hold off.

The proposed initial cost of £1m is a small price to pay for the opportunity to preserve BPL's market position and the benefit that brings to the NHS while leaving time to examine more appropriately BPL's longer term future. If the judgement of BPL is wrong and the market collapses anyway,. then that small extra cost is overwhelmed by the major funding requirements identified under scenario 2a.

In this scenario, BPL has assumed that there would still be some loss of export business as in scenario 1 and hence the total funding requirement for 1998/99 would be £18m. However, this may be a pessimistic assumption on exports which would lead to a funding requirement of perhaps £2m or more less than this forecast.

For 1999/2000 funding requirements would be very dependent on developments on nv-CJD as for scenario 1.

If there are no further recalls and concerns over nv-CJD reduce, then UK Factor VIII and Factor IX sales would continue to decline in 1999/2000 and 2000/01. However, increasing UK Intravenous Immunoglobulin (Vigam) sales together with increased exports of all products would compensate and BPL's funding requirement would start to reduce slowly.

If there are no further recalls but there is continuing uncertainty over nv-CJD then UK Factor VIII and Factor IX sales will fall faster and slower growth of UK Vigam and exports will fail to compensate. Total revenue will fall and funding rise leading to concerns over BPL's viability if it has remained an independent entity.

If there is a further recall and concerns over nv-CJD increase the effect will be as for scenarios 2a and 3 with closure inevitable.

Very approximate projections are given in the table below:

	1998/99 Funding Requirement	1999/2000 Funding Requirement	2000/01 Funding Requirement
No recalls in 1998/99	£18m		
No further recalls & reduced nv-CJD concerns		£17.5m	£17m
No further recalls but continuing concerns		£23m	£24m
A further recall and increasing concerns		£26-32m & BPL closure	-

Scenario 3

This assumes that Ministers determine the risk of transmission of nv-CJD from blood products is sufficiently high that they should "fund fully" recombinant Factor VIII for all (and Factor IX when licensed). It does however also assume that the risk is not deemed sufficient to determine that BPL plasma should not be used for products but allows the market to choose without financial constraints.

In this case the recombinant Factor VIII manufacturers will move rapidly to direct product to the UK from other areas to secure their market position. Increasing product availability would be expected each quarter through 1998/99 to achieve a 90% penetration by early 1999.

This move will also be seen publicly as implying that the use of BPL products in general would incur an unacceptable risk. UK albumin and immunoglobulin sales would be lost as would be a very substantial part of the export business (see assumptions in Appendix C). In this scenario the BPL business goes into rapid decline during 1998/99 with a revenue support requirement of £25m and an ongoing support thereafter of £32m, ie similar to scenario 2a. As for scenario 2a, there would be a need to destroy surplus plasma as only 380T would be fractionated in 1998/99.

As for scenario 2a there would be no option but to close and/or sell BPL and destroy NBS plasma as it would be unsaleable.

The additional cost of funding recombinant Factor VIII in 1998/99 is £20m rising to £35m in a full year (£30m excl.VAT).

Scenario 4

This assumes UK plasma is deemed to carry an unacceptable risk and no plasma products should be manufactured from it. In these circumstances there is an option to base the business on purely purchased plasma and intermediate raw materials. It would not be possible immediately to purchase the full 600 tonnes of plasma that BPL currently consumes but it would be possible to purchase sufficient plasma to meet UK albumin and immunoglobulin needs together with the cryoprecipitate to boost Factor VIII availability. The plasma would almost certainly have to be from paid US donors. BPL believes it could purchase that raw material and meet forecast UK needs while keeping within the requested PES funding of £10.7m for 1998/99.

This would keep BPL operational while considering it's future and there would be very substantial surplus capacity to fractionate on behalf of other manufacturers or countries. However, it would leave the NBA with 600 tonnes of plasma to dispose of and a financial shortfall of £23m per year. The cost of the actual disposal of plasma would be less that £1m per year.

There would of course be no logic in the NBA retaining any financial interest in BPL under this scenario unless it was believed that the nv-CJD concerns would be removed quite quickly and allowing NBA plasma to become an acceptable raw material once more. However, the lost export business would take time to recover with a consequent substantial funding need.

BPL FORECASTS

£m	1997/98	1998/99	1999/2000	2000/01	2001/02
Budget 1997/98 Total Revenue BPL I&E Deficit Revenue Funding	53.6 9.5 9.5				
Latest View 1997/98 post nv-CJD Total Revenue BPL I&E Deficit Revenue Funding	55.5 8.4 8.4				
Long Term Forecast pre nv-CJD Total Revenue BPL I&E Deficit Revenue Funding	56.4 7.6 7.6	63.0 6.2 6.2	64.3 4.8 4.8	61.5 6.9 6.9	59.5 6.6 6.6
PES Bid (et Feb 1997) Total Revenue BPL I&E Deficit Revenue Funding	53.6 9.5 9.5	54.9 10.7 10.7	 10.0 10.0	 10.5 10.5	

NOTE: In long term forecast the reduction in sales of UK Factor VIII is more than compensated for by high growth of UK and Export sales of Intravenous Immunoglobulin together with increases in Factor VIII exports to developing countries.

ANNEXE E

ANNEXE F

BPL
Bio Products Laboratory

BPL PRODUCT RANGE AND ALTERNATIVE SOURCES OF SUPPLY FOR THE UK MARKET

SUMMARY

In general alternatives to BPL plasma products are available but, in some cases, these alternatives would have to be supplied on a named patient basis i.e. they do not have UK Marketing Authorisation. In the cases of special coagulation Factor XI, an alternative is not readily available, but only a small number of patients is involved and generally their requirements can be predicted in advance of actual needs.

It is essential to note that BPL has a large share of the UK market in all the products it supplies. The smallest share (20-25%) is in Intravenous Immunoglobulin for which demand is growing rapidly throughout the world leading to some shortage of supply. Any major shortfall in BPL supplies could not be filled immediately by imports and product shortages would occur.

On Varicella Zoster immunoglobulin, there could be significant difficulties in identifying adequate alternative supplies. BPL has not been able to meet PHLS demand over the last year due to a shortage of plasma but a programme is currently in hand within the NBS to resolve that issue. Overall, no patients would die as a direct result of BPL withdrawing supplies although PHLS would have to advise on the consequences of little or no VZ immunoglobulin being available.

COAGULATION FACTORS

Factor VIII

BPL offers a monoclonally purified Factor VIII, Replenate, and an intermediate product, 8Y. Recombinant Factor VIII is available on a fully licenced basis from Baxter and Bayer, and Centeon also re-sells products purchased from Bayer and Baxter. In addition, a recombinant product from Pharmacia and Upjohn / Genetics Institute is under clinical trial. Centeon and Alpha currently supply licenced high purity plasma derived products in the UK.

Factor IX

BPL offers two products, a high purity single Factor IX, Replenine, and 9A. 9A is an intermediate purity prothrombin complex product which contains coagulation Factors II, IX and X. It has a transitional licence and is now mainly used for Warfarin reversal and replacement therapy for Factors II and X deficient patients.

Licensed alternative high purity Factor IX products are available from both Centeon and Alpha. There is no licensed alternative prothrombin complex but a number of European manufacturers make four factor prothrombin complexes (factor VII in addition to II, IX and X) which could be supplied on a named patient basis in the UK.

A recombinant Factor IX from Genetics Institute is expected to be licensed in Europe in 1998 but product availability is expected initially to be very limited.

Factor VII — no patients — Useage rate / annum. —

BPL offers an unlicensed Factor VII product for the limited number of users in the UK. Immuno also make a product which is unlicensed in the UK but they are very short of it. Other possibilities are recombinant 7A from Novo Nordisk which is very expensive and only has a short half-life. The other alternative is a four factor prothrombin complex as mentioned above.

Factor XI

BPL makes an unlicensed factor XI which it supplies into the UK and in very limited quantities, under very special circumstances, overseas. The only other company to offer Factor XI at all is LFB in France but their supply is uncertain and there are substantial concerns over thrombogenicity. Alternatives are DDAVP and fresh frozen plasma.

Factor XIII

BPL's product is unlicensed and there is no licensed alternative in the UK but Centeon make very large quantities of a product which is licensed in a number of countries in Europe and Japan.

Anti-Thrombin III

BPL's product has a transitional licence and there are no alternative licensed products in the UK but Centeon, Pharmacia & Upjohn and possibly others can offer products, which are licensed elsewhere, on a named patient basis.

von Willebrand Factor

BPL offers 8Y as a treatment for von Willebrand Disease and there is an alternative, Haemate P, available from Centeon. The majority of patients are normally treated with DDAVP; the severe patients could be treated with cryoprecipitate.

ALBUMIN — Annual Useage – Gestated how many infusions given —

BPL offers 4.5% and 20% solutions of Albumin and there are other licensed UK suppliers such as Immuno (Baxter) and Alpha.

IMMUNOGLOBULINS

Intravenous Immunoglobulin

BPL offers both a freeze-dried product, Vigam-S and a liquid version, Vigam Liquid. Alternative licensed products are available from Novartis (Sandoz), Alpha, Octapharma, Baxter and Bayer.

Intramuscular Products

Normal intramuscular immunoglobulin is used mainly for protection against Hepatitis A for overseas travellers. In addition to BPL's product, supplies can also be obtained from

Immuno and Pharmacia & Upjohn. These products can also be used for virus infection complications where the Hepatitis A vaccine, Havrix, is not appropriate.

Anti-D

BPL's product currently has a transitional licence. Immuno has a licensed product in the UK but only have limited supplies. Cangene from Canada are understood to be moving towards a UK licence for their product already licensed in N.America and some European countries. Anti-D is generally short across the world.

Varicella Zoster

BPL's product is licensed. There is no other licensed product and no current vaccine although one is on trial in the USA. The product is generally short worldwide with a limited number of manufacturers. It would be possible to use intravenous immunoglobulin as an alternative as that contains varicella zoster antibody but very large volumes would be needed to meet the necessary dose which would make that alternative expensive and not an easy option.

Tetanus

Immuno currently offer a licensed product in the UK.

Hepatitis B

There is no UK licensed alternative to the BPL product. There are however products licensed in Europe which could be supplied on a named patient basis.

Rabies

We believe unlicensed product would be available from several European sources.

NOTE: Supplies of product from PFC have all been excluded from the above.

R C D Walker
12January 1998