Annex B

FUTURE SUPPLY OF PLASMA DERIVED PRODUCTS TO THE NHS

Introduction

1. The remit for the BPL review requires consideration of "how the NHS in England and Wales can be provided by BPL with a secure supply of sufficient, competitively priced product in the event of global shortage". This is a key criterion for the Department in judging the acceptability of any option for the future of BPL. Furthermore, any restrictions we wish to place on a future BPL partner around security of supply will at least partially determine structural options and may impact on the value to be achieved from the reconfiguration of BPL. It is therefore essential that we have a clear and common understanding about what "security of supply" really means and the extent to which it is achievable in practice.

2. Security of supply is much more of an issue for blood products than for pharmaceutical products in general. As biologicals, the production of plasma-derived blood products is subject to increasingly rigorous regulation by the MCA and the US Food and Drugs Administration (FDA). Both authorities have the power to shut down plants if they fall seriously short of the required standards, and recent shut-downs in the US have led to world-wide shortages of some products.

3. This paper is therefore structured to focus on two areas concerning security of supply:

- the likely future demand for plasma derived products from the UK;
- the mechanisms by which the level of security required could be provided in the future.

The Likely Future Demand for Plasma Products from the UK

5. BPL has produced a paper on likely future demand for plasma based products (attached). This assumes that:

- sales of plasma-derived Factor 8 & 9 will decline to very low levels in the UK due to the increasing use of recombinant products for the treatment of haemophilia.;
- world wide surpluses of albumin, the use of which is declining, means that it unlikely that the UK would ever run short of this product.

The only products that could suffer from problems of supply in the future are therefore identified as immunoglobulins and some more rarely used clotting factors such as Factor 7 and Factor 11.

BPL supplies three types of immunoglobulin:

- ***Intravenous immunoglobulin***; critically used by people with immune deficiency but increasingly for a variety of other uses. BPL is currently the market leader (with about 50% of the supply market) for this product in the UK. As such BPL is capable of providing enough Immunoglobulin to meet the needs of all immune deficient patients in the UK who account for around 25-33% of the total current demand.

- ***Anti-D immunoglobulin***; used to treat approx 90,000 pregnant Rh negative mothers per year. BPL is currently the dominant supplier to NHS and private hospitals for this essential use.

- ***Specific Immunoglobulins***; BPL directly supplies the Public Health Laboratory Service (PHLS) with Hepatitis B, Varicella Zoster and Rabies Immunoglobulin and the Ministry of Defence (MoD) with Rabies Immunoglobulin. BPL is the sole licensed supplier of Hepatitis B, Varicella Zoster and Rabies Immunoglobulin to the UK (apart from PFC who supply small quantities of Hepatitis B and Varicella Zoster in Scotland and N.Ireland) and their supply to the PHLS and MoD is therefore sensitive.

6. It needs to be ensured that all these types of immunoglobulin, and the more rarely used clotting factors, continue to be available to essential UK users under any new ownership arrangement for BPL. It is proposed that the future needs of PHLS and MoD for specific immunoglobulins should be met through contracts between these bodies and BPL. However, we need to ensure that sufficient supplies of these products are also available to NHS hospitals.

How Security of Supply could be Provided in the Future

7. This section considers how security of supply can be ensured for Immunoglobulin in the future under new ownership arrangements. This is considered in two parts:

- Firstly, defining what security of supply for plasma products means

- Secondly, outlining the options for providing security of supply in the future.

Defining Security of Supply for Plasma Products

8. Examining the nature of plasma product supply reveals that there are two key resource constraints involved:

- ***plasma supply to the UK***; the UK is dependent on other countries for the supply of plasma since the ban on the use of UK plasma. At the moment BPL has two year rolling contracts with plasma suppliers in the USA which are renewable annually; meaning that BPL has at least one year's guaranteed plasma supply at any time. In addition, BPL is currently building up a further 60 day stock within the plant. It should be stressed that BPL has to work very hard to obtain sufficient supplies of plasma from the US and that there may be further demand for US

plasma if other European countries, notably France, switch to imported plasma. There is therefore no long-term security of supply of plasma [as is now the case];

- ***fractionating capacity***; a licensed fractionating plant with sufficient capacity is required in order to break the plasma into the proteins required. Currently access to such capacity is assured in the UK by the public sector owning BPL.

9. Both of these constraints will need to be addressed when considering future ownership scenarios for BPL and the options for doing this are presented below.

Options for Providing Security of Supply in the future

10. Presented below are the options that address the two key resource constraints for security of supply.

Options for Addressing Future Plasma Supply to the UK

11. As highlighted above, under current arrangements BPL is always contracted for at least one year's supply of plasma at any time. This means that any short term changes in the plasma market (such as further countries being unable to use their plasma supply because of the occurrence of vCJD) are unlikely to immediately affect plasma supply to the UK. (Unless US plasma becomes unusable or the US government takes some emergency action to ensure all plasma is directed to home use.) However, in the longer term, difficulties in plasma supply will inevitably push the price of plasma up.

12. Any changes in plasma supply, such as price increases, are therefore unavoidable under any ownership option including retention in the public sector. But in order to ensure complete replication of current security of supply it is proposed that under new ownership arrangements BPL must be required to contract with US plasma suppliers using contract lengths that are no shorter.

Options for Ensuring Sufficient Fractionation Capability Exists

13. In order to turn plasma into products access is required to an appropriately licensed fractionating plant with sufficient capacity. The UK currently assures such access by retaining ownership (which brings other risks). This access could be protected under future ownership scenarios by three options outlined below:

- ***Requiring pre-emptive supply to the UK market***; under this option the new owners of BPL would be required to give assurances of pre-emptive supply to the UK's immunoglobulin needs (this would need definition but is likely to be based on immune deficients, Anti-D, PHLS and MOD requirements.) Such commitments from the new BPL are unlikely to be particularly onerous in volume terms. BPL's current export contracts, which recognise that in times of supply difficulty the UK market will always gain preferential supply, provide a precedent for such an arrangement.

- ***Corporate governance of the New BPL***; the Public Sector can affect the future preferential supply to the NHS by ensuring that it has such powers via the

governance arrangements of the new organisation, this might be in the form of the public sector:

- Maintaining a majority share of the new BPL
- Holding a golden share in the new BPL
- Designing a governance structure which allows it sufficient influence on future decisions about pre-emptive supply (eg a majority of board seats)

- ***Use of PFC as a back up***; PFC (the Scottish fractionator) has only limited fractionating capacity - 100 – 130 tonnes per annum. They make all immunoglobulin types except rabies, and could perhaps supply limited quantities of product to hospitals in England & Wales in an emergency. However, they could not make enough immunoglobulin for immune deficient patients in the UK.

14. In summary, it can be seen that by applying one or more of the options above it is possible to assure security of supply without retaining ownership of the fractionating capacity. It should of course be recognised that each of these different options do however bring some additional cost to the future arrangements for BPL.

Conclusion

15. Overall it can be seen above that ownership of the fractionator is not the only method for ensuring security of supply. By careful application of the options above it will be possible to provide security of supply equivalent to that currently enjoyed. The proposed options for doing this are outlined below.

16. As indicated above the security of plasma supply will be equal under any ownership option as long as the new BPL is required to engage in contracts of the same length as those currently held by BPL.

17. In order to provide current levels of security of fractionating capacity it is proposed that a pre-emptive supply agreement for the UK's minimal immunoglobulin requirements (which need to be defined) be included as the foundation of any future ownership option. This should be further re-inforced, if possible, by an appropriate 'golden share' governance structure that allows the public sector some control over the new BPL. In addition, PFC may be able to provide some limited stop-gap provision.

Charles Lister
Department of Health
November 2000

BPL
Bio Products Laboratory

BPL PRODUCT RANGE AND CONTINUITY OF SUPPLY

BPL supplies a wide range of products to the NHS in England and Wales and in some instances supplies the entire UK needs. The products fall into three main product ranges, namely clotting factors, albumin and immunoglobulins. For the major products in these three groups, there are several alternative suppliers and the trend in some cases is away from plasma derived products to alternatives.

The situation on the major product groups and minor products is as described below.

CLOTTING FACTORS

The major products to treat Haemophilia A and Haemophilia B are Factors VIII and IX. Several suppliers are already supplying licensed products in the UK in direct competition with BPL's products. However, the demand for these plasma derived products is declining as the products of choice are recombinants from three suppliers in the case of Factor VIII, and one supplier in the case of Factor IX. With BPL's current plasma supply, it could only meet around 45% of the UK's Factor VIII needs but has a very large surplus of Factor IX if required to meet any likely any future demand for Factor IX.

It is assumed that BPL sales of plasma derived Factor VIII and IX in the UK will continue to decline to very low levels over the next few years, but product could be diverted from export markets if required as BPL will continue to sell their products to satisfy growing needs in developing countries.

Other Clotting Factors

Factor VII

BPL offers an unlicensed Factor VII product for a limited number of users in the UK on a named patient basis. Baxter Immuno is the only other supplier, again with an unlicensed product. There are very few users of this product worldwide and it is therefore made available on a compassionate basis. There are other possibilities. Recombinant 7A from Nova Nordisk, which is very expensive and only has a short shelf life. A four factor prothrombin complex, which contains Factor VII in addition to II, IX and X. This is available from a number of European manufacturers although not licensed in the UK.

Factor XI

BPL makes an unlicensed Factor XI which is supplied to UK patients on a named patient basis and again supply is in very limited quantities overseas under very special circumstances. The only other company to offer Factor XI is LFB in France, but again this product is unlicensed.

Anti Thrombin III

BPL's product currently has a transitional licence but is likely to be moved to supply on a named patient basis. There is only a small number of users in the UK and there are other products licensed in Europe which could be supplied to the UK on a named patient basis.

von Willebrand Factor

BPL offers its intermediate purity Factor VIII, 8Y, as treatment for von Willebrands disease, but this product seems to be less effective since the conversion to US plasma and the majority of patients are now treated with Hemate B available from Aventis Behring. The majority of patients are normally treated with DDAVP.

ALBUMIN

BPL provides two grades of albumin, namely 4.5% and 20% solutions. There are several other licensed suppliers of albumin to the UK, but there has recently been a strong move to non-plasma alternatives due to concerns over albumin and there is now a very large worldwide albumin surplus, which means the likelihood of the UK ever running short of product is extremely small.

IMMUNOGLOBULINS

Intravenous polyvalent immunoglobulin is a product with a wide and growing range of uses for which there are in some cases no alternative products available. The UK market is currently supplied by more than six manufacturers but demand is growing and shortages are a common feature. The most important group of patients dependent on this product is that suffering from a range of immune deficiencies. This group of patients currently accounts for between one-quarter and one-third of UK immunoglobulin usage.

Specific Immunoglobulins

Anti-D

BPL is currently the major supplier of Anti-D immunoglobulin in the UK with two other licensed suppliers, namely Baxter Immuno and Cangene. There is currently surplus of Anti-D plasma in the USA and no shortage is anticipated over the next few

years at least, so no shortage of the immunoglobulin is expected even allowing for growth in demand for ante-natal prophylaxis.

Tetanus

BPL is the major supplier of tetanus immunoglobulin in the UK with Baxter Immuno also offering a licensed product.

Hepatitis B

BPL is the sole supplier of a licensed intramuscular product supplied to the PHLS. BPL also supplies an unlicensed intravenous product on a named patient basis, largely used for liver transplantation.

Varicella Zoster

BPL is the sole supplier of this licensed product and supplies all of it to the PHLS.

Rabies Immunoglobulin

BPL is the only licensed supplier of this product to the UK and supplies the PHLS and the Ministry of Defence.

SECURITY OF PRODUCT SUPPLY FROM BPL IF OUTSIDE THE NHS

There seems no case for any contractual arrangement obliging BPL to make any formal commitment to continuity of supply to the UK for Factors VIII and IX.

In the case of von Willebrand factor, again unless BPL can produce a more effective product which it has in development, there is no case for seeking a contractual commitment.

For the other special coagulation factors, the situation is somewhat sensitive as the products are unlicensed and supplied on a named patient basis. BPL has discontinued supply of such unlicensed products whenever a licensed alternative has become available and would expect the MCA to support such a move. However, it should be possible to cover the supply of these special factors in a contract.

Albumin

There is no argument to seek any commitment from BPL to supply the UK market.

Immunoglobulin

Intravenous immunoglobulin for immune deficients will always be an extremely sensitive area. BPL can be expected to seek to continue to be the market leader in the UK on the assumption that prices are not significantly below those generally available in overseas markets. In those circumstances it would not be unreasonable to require that BPL commit to supply sufficient immunoglobulin to the UK market to meet the

entirety of the immune deficient needs, even though that product may be at any time spread across a wide range of uses. Hence, in the event of severe shortage, that product could be redirected to essential users only. BPL would expect to grow its immunoglobulin business worldwide very substantially over time and hence such an obligation would be decreasingly onerous over time.

Other Specific Immunoglobulins

For other than Anti-D, it would seem most logical for there to be a contract between BPL and the PHLS, where BPL is committed to supply the entire needs of the PHLS based on a three year forecast, updated annually. The total value of this contract would be around £3 million a year and some appropriate formula could be devised to control the prices if the PPRS were not deemed appropriate. The PHLS may not wish to get involved in tetanus but if the NHS wants to ensure that product is available and committed, then someone has to make sure that BPL and/or Baxter Immuno make available sufficient product to meet the small needs for the NHS.

In the case of Anti-D, this product is clearly extremely sensitive with demand likely to grow substantially as ante-natal prophylaxis is introduced. Some may view ante-natal prophylaxis as being a bit of a luxury in case of product shortage and hence if a contract were signed to supply, for instance, all the post natal needs, then that would probably be acceptable.

PFC's POSITION

In the case of immunoglobulin, both intravenous and specific, it should be remembered that PFC are also suppliers of all but rabies which they purchase from BPL. They could undoubtedly, over a comparatively short period of time, satisfy all the specific immunoglobulin demand although Anti-D might put them under some pressure. They also supply intravenous immunoglobulin to a wide range of users in Scotland and Northern Ireland. So PFC could provide a partial backstop were there any difficulties in supplies from BPL.

R C D Walker
15 November 2000