Chapter 9

Options for increasing competition for plasma fractionation

The Review has considered three potential options that could deliver fractionation services for Australia in future years. These are:

1. Maintenance of the current arrangements involving fractionation of Australian plasma in a domestic fractionation facility.
2. Open tender for the fractionation of all Australian plasma.
3. Open tender for the fractionation of part of the plasma collected in Australia, with a defined quota being fractionated in Australia.

Option One

Australia's current fractionation arrangements, agreed by the Australian Health Ministers' Conference (AHMC), provide for the fractionation of all Australian plasma onshore in Australia, by CSL Bioplasma. The arrangements also provide for the importation of plasma derived products that either are not manufactured domestically or, as in the case of intravenous immunoglobulin (IVIg), are required to augment domestic supply where plasma collected in Australia is insufficient to meet clinical demand for a particular product.

It is necessary to distinguish between CSL Bioplasma, which is a stand-alone fractionation operation located at Broadmeadows, Victoria, and CSL Limited. CSL Bioplasma has been Australia's national fractionator since 1953 and is a business operating unit of CSL Limited. Other business operating units of the CSL Group include CSL Behring. The CSL Bioplasma plant at Broadmeadows is dedicated, as a first priority, to the fractionation of Australian plasma and is separate from the much larger CSL Behring 'centres of excellence' model, which is described elsewhere in this Report and which serves international markets.

Option Two

This option involves an open tender process to secure the fractionation of all plasma collected in Australia. It would involve the National Blood Authority (NBA) entering into a contract with a domestic sponsor representing an overseas fractionator, although it may be possible to have this contract executed as a tripartite arrangement that could enhance the legally enforceable relationship between the NBA, representing Australia's Commonwealth, state and territory governments, and an overseas fractionator. Alternatively, an agreement could be a bilateral arrangement between the NBA and the domestic sponsor, with an offshore principal providing a financial guarantee of performance, to underpin the agreement. It is possible, of course, that CSL Bioplasma could secure such a tender; in this case, most of the circumstances of Option One would apply, although against the background of a competitive tender process.

A prerequisite for participation in an Option Two tender would be the completion of registration procedures with the TGA for all of the products involved, prior to contract implementation.

Unlike the standing offer arrangements where the supplier undertakes to provide supply of a product configured to the needs of the international market (e.g. strength and pack size), a tender for the fractionation of Australian plasma would include product specifications set by the NBA and similar to those contained in the schedules to the existing Plasma Products Agreement (PPA).

Thus, a tender participant may need to develop and register entirely new product forms in order to meet Australian specifications. This process could take up to two years to complete, particularly if clinical trials are required to support the registration dossier. On the other hand, if a tender participant already has products registered in Australia that meet Australian requirements in terms of strength, pack size and presentation, then only a variation to the existing registration, involving a revised Plasma Master File, would be required; the resulting registration process could be as short as three to six months.

Option Three

The third option involves a split of Australian-sourced plasma resources between an overseas fractionator or fractionators, and a domestic fractionator. This option would cater in part for a government policy position that may seek to maintain, for national interest reasons, a domestic fractionation capacity while opening the market to a competitive process.

There would be a number of subsidiary scenarios available for consideration under this option, including:

1. The tendering for a minimum viable amount of plasma (say 48 000 litres annually) for overseas fractionation into IVIg and plasma derived Factor VIII, with the remainder of the supply being allocated to CSL Bioplasma for the manufacture of all fractionated products in the current domestically produced range.
2. The splitting of the total plasma collection into two allocations – one for overseas fractionation into all products and the other for fractionation by CSL Bioplasma into all products. This alternative would see the production of hyperimmunes continuing in Australia.
3. The splitting of the total plasma collection across a number of fractionators, including CSL Bioplasma, with contracts being awarded according to best value for money for each individual product.

A possible benefit to Australia from any one of these arrangements would be that it would allow the National Blood Authority to benchmark prices on the basis of bids received from all fractionators.

Criteria

Each of the three options has particular advantages and disadvantages, and these will be explored further in this chapter. The plasma fractionation industry is a complex sector that calls for careful evaluation and weighting of multiple criteria when considering options. Arrangements for the fractionation of Australian plasma require consideration of matters well beyond those associated with value for money, although this remains one of the foremost issues to be taken into account.

In regard to the concept of Australia having a domestic fractionator, the Review observes that there is only one fractionation plant in Australia. The Review has attempted to draw the international industry on the potential for a second plant to be constructed. This attempt has not resulted in any definitive responses but it is prudent to assume for the purposes of this report that Australia will continue to host only one fractionation plant.

The criteria identified by the Review as being appropriate for testing each of the options are as follows:

- security of supply, and logistics
- product safety, quality and efficacy
- yield
- expenditure and value for money
- plant capacity
- product range
- product registration
- market share and competition
- legislative issues
- domestic industry and research
- regional relationships
- contract duration
- contract enforcement
- product liability.

The most important issues bearing on public confidence in the Australian blood supply are security of supply as well as product safety, quality and efficacy. Yield has the potential to impact heavily in terms of reducing the supply of IVIg derived from Australian plasma and increasing reliance on imported products manufactured from overseas-sourced plasma. Another important issue is the national strategic value of a domestic fractionation facility.

Security of supply, and logistics

The Review has concluded that the greatest degree of security available lies in the maintenance of a domestic source of supply, because of the relative remoteness of Australia from major global centres of population and because of the existence of long lines of supply between Australia and alternative fractionation sites, which in turn pose additional levels of risk to supply. The Review appreciates that Australia's

pharmaceutical product needs are met in large part by imports, but recognises that blood and blood products represent a special case for consideration. The Commonwealth Procurement Guidelines acknowledge this special case by exempting from the Mandatory Procurement Procedures the procurement of blood plasma products or plasma fractionation services.[1]

In considering the supply of plasma and plasma derived products in Australia, there are multiple factors to be addressed, including the need for maintenance of cold chain conditions throughout the supply and manufacturing arrangements; the scarcity and irreplaceable nature of the Australian plasma collected for fractionation, and the need for certainty in the continuity of supply of finished products. Domestic fractionation within Australia clearly offers the best guarantee of security of supply when all factors are taken into account. In terms of logistics, the key points that have been considered are:

- length of lines of supply
- number of transhipment points
- duration of shipments
- exposure of shipments to acts of neglect, terrorism or sabotage
- ability of the Therapeutic Goods Administration (TGA) to apply direct controls over supply arrangements

The amount of plasma that needs to be transported for fractionation is measured in tonnes. Total volume is currently in excess of 300 tonnes per annum. Projected estimates for 2015–16 indicate a total tonnage of between 600 and 700 tonnes. Transporting this volume of plasma, or even a proportion of this volume, by airfreight to either North America or Europe is considered to be impractical. Sea shipment appears to be the logical option, and this view is shared by all but one overseas fractionator. Depending on the overseas fractionator involved, shipping times could vary from between 30 to 40 days after sailing. Frequency of sailings to given overseas ports is an additional consideration. Land handling would be required at both ends of the shipment process and would increase the number of transhipment points.

In considering the feasibility of overseas fractionation, the Review has taken into account increased risks associated with long lines of supply, special shipping conditions and multiple transhipment points.

This point needs to be qualified, however, with the observation that no supplier – whether domestic or offshore – is immune to disruptions to processing and transportation. It is more a question of degrees of risk relative to each situation.

A change to a system whereby all of Australia's plasma was fractionated overseas would require a considerable change in logistical arrangements, involving both internal lines of supply within Australia and external arrangements.

The transportation of Australian plasma to CSL Bioplasma is currently handled by the Australian Red Cross Blood Service (ARCBS). This arrangement could continue, with a different central collection point being nominated by a successful tenderer. Alternatively, a successful tenderer may undertake internal logistics within Australia,

1 *Commonwealth Procurement Guidelines – January 2005*, Financial Management Guidance, no. 1, Department of Finance and Administration, Canberra, 2004, p. 46 (Appendix B, item 13); also available online at <http://www.finance.gov.au/procurement/docs/CPGs_-_January_20051.pdf>.

including the pick-up of plasma stocks from ARCBS collection points; the plasma would then be consolidated for international shipment. The choice of arrangements would depend on demonstrated efficiency and cost benefits. Onwards shipment to the overseas fractionation site would be arranged by the successful tenderer, and the associated costs and assumption of risks would be factored into the overall fractionation fee-for-service.

All overseas fractionators contacted by the Review have indicated that a minimum 60-day withholding period (measured from the date of collection) is applied for safety reasons to all plasma received. The withholding is for the purposes of 'look-back' – a process that enables suspect plasma to be identified and removed from the starting pool batch prior to fractionation, if a donor is discovered to have an infection risk subsequent to the time of donation.

In Australia, the domestic fractionator is not required by the TGA to apply a withholding period. It would be a matter for negotiation as to whether there would need to be a withholding period applied to Australian plasma fractionated overseas.

It is of note that any withholding period applied in this case would more than cover the amount of time required for the sea shipment of plasma from Australia to the overseas fractionation site. It is estimated that the minimum turnaround time between plasma collection in Australia and the availability of finished products to Australian patients would be between six and nine months. At present the turnaround between plasma collection and delivery of finished product is on average ten weeks.

The length of turnaround time associated with the overseas fractionation of Australian plasma would hold implications for continuity of supply. An additional stockholding in the National Reserve, equivalent to at least six months' demand for all plasma products required for use in Australia, is considered to be an essential requirement in the event that all of Australia's plasma is sent overseas for fractionation.

While this would be a once-only requirement, it would nevertheless pose an additional potential burden on the National Reserve and would be difficult if not impossible to meet from domestic sources, given the scarcity of Australian plasma. It seems likely that the only way in which this requirement could be met is through the acquisition of finished products made from overseas plasma. This scenario has implications in terms of Australia's policy of self-sufficiency and could result in undesirable impacts on patients and clinicians, as a consequence of brand switching.

The cost of acquiring on the open international market an additional six months' inventory of the key plasma products (IVIg, albumin, Factor VIII and Factor IX) could be as high as A$75 million, based on prices in the current National Supply Plan and Budget. The procurement of the necessary quantity of product (equivalent to the output from up to 150 000 litres of plasma) would potentially be undertaken by the National Blood Authority through the mechanism of a single Request for Tender (RFT) process.

The prospect of such a large acquisition also raises the prospect of two rounds of brand switching in a relatively short period of time – a process strongly disfavoured by clinicians and product recipients alike, for sound clinical reasons.

The return of finished goods from an overseas fractionator to Australia, under Option Two or Option Three, would need to be undertaken by airfreight. This would limit the turnaround time between collection of plasma and availability of finished products in Australia. The alternative, sea shipment (which is favoured by one fractionator), could effectively add a further two to three months to the turnaround time. Under existing arrangements, an order for IVIg placed under Australia's contingency standing offer agreement with a European fractionator takes a minimum of two to three months to be filled. Again, the cost of returning finished products to Australia would be factored into the fractionator's fee-for-service.

Distribution of finished products to hospital blood banks could be undertaken either via the ARCBS network, as is now the case, or directly by the overseas fractionator's Australian sponsor, depending on the relative costs and efficiencies of the arrangement (but taking due account of gatekeeping functions presently performed by the ARCBS in conjunction with jurisdictional authorities).

Under existing arrangements, CSL Bioplasma is required to provide an alternative source of product supply in the event of a disruption to domestic production for any reason. The contingency requirement is addressed by means of a guarantee of product supply from CSL Bioplasma's sister organisation CSL Behring. This important security of supply guarantee effectively reduces to an acceptable level the supply risk associated with single-site fractionation. A similar undertaking from an alternative fractionator would be necessary in the event of overseas fractionation.

A contract for the fractionation of all or part of Australia's plasma at an overseas location would amplify the level of inherent risk associated with the supply of finished plasma products. Of particular concern is the possibility of loss – through damage, neglect or criminal act – of an entire container (eight tonnes) of Australian plasma, and the effect that such a loss would have on continuity of supply.

Due to the long lead times involved in collecting plasma domestically, it would not be possible to replace such a loss promptly, and resort to a contingency arrangement would be required. A similar risk attaches to the return of finished product to Australia (which would presumably be by airfreight). Here the risks of loss or damage relate particularly to loss of cold chain integrity at transhipment points or in airport handling – not unknown occurrences.

Under current arrangements, as noted above, the ARCBS is responsible for the delivery of starting plasma from collection sites to the domestic fractionator. This is achieved using a variety of transportation methods, including road transport and airfreight. Many of these arrangements are a legacy from the time when each state or territory branch of the ARCBS was a discrete entity.

CSL Bioplasma carries the responsibility for the return of finished products to ARCBS for onwards supply to hospital blood banks. In practice, CSL provides some of the warehousing function to support these arrangements, noting that distribution in Australia involves large distances to serve relatively small populations.

CSL has provided the Review with a submission that explores the possibilities of rationalisation of current distribution arrangements. The Review has not made a detailed assessment of distribution efficiency but believes that this issue should be further investigated.

In any case, under Option Three the ARCBS would be faced with the prospect of operating duplicate systems for the bagging, bar coding, storage, handling and transport of the plasma collection. Under this option, the ARCBS would also be required to provide for the handling and distribution of two brands of some or all of the finished product range. This duplication, while entirely feasible, represents yet another new element of risk arising from the possibility of human error.

The introduction of a second or third fractionator would involve the need to set up in Australia one or more consolidation points where international shipments of plasma could be assembled and despatched. Freezer storage (circa –20° to –25°C) would be required at each location. International forwarding would require the use of specialised containers capable of reliably maintaining cold chain conditions. Continuous temperature monitoring would be required throughout the forwarding process, and the plasma shipments would need to be checked on arrival at their destination.

The additional costs of these arrangements would be factored into the tendered price for overseas fractionation. In the context of overall fractionation costs, additional transportation costs are a marginal consideration but it is the additional risk involved that represents the greater concern.

The loss of plasma or finished plasma products in transit between Australia and an overseas fractionator is likely to be insurable, although it is not likely that full coverage could be obtained. The cost of insurance would be factored into the fractionator's fee-for-service. But the physical loss of plasma or finished plasma products cannot be compensated for in economic terms alone. The point is that Australian plasma is regarded by many stakeholders as a unique, scarce and irreplaceable resource, as are the products manufactured from it.

It is nevertheless true that reliance upon a single fractionation site carries a remote but severe risk of loss through plant breakdown, fire or sabotage. As noted earlier, under present contractual arrangements, whereby Australia relies on CSL Bioplasma for the provision of most of this country's plasma product needs, there is a contingency arrangement in place such that, in the event of a major disruption to supply, plasma products would be provided by CSL Behring.

In reaching a conclusion on the issue of security of supply, the Review has taken account of a wide range of factors, including those that inspire confidence in the global nature of the fractionation industry as well as those particular to Australia's geographic location, remote as it is from Northern Hemisphere concentrations of the fractionation industry. In respect of security of supply, the Review favours Option One because, given the contingency arrangements that are in place, it provides the best guarantee of supply security.

Product safety, quality and efficacy

As described in Chapter 8, the Therapeutic Goods Administration regulates the safety, quality and efficacy of both plasma collection in Australia and the fractionation of Australian plasma into finished therapeutic products. The possibility of enhancing the regulatory process in regard to plasma derived products under the various options is canvassed elsewhere in this report.

There are regulatory advantages to the continuation of the fractionation of Australian plasma within Australia. These are:

- continuing close oversight by the TGA of the entire supply chain, from blood and plasma collection, through the transportation and the fractionation of plasma, to delivery of finished products to hospital blood banks
- ability of the TGA to enforce, as necessary, regulatory requirements and inspections and to apply sanctions directly and within an Australian jurisdictional context, as opposed to relying on a third party regulator in an overseas country or on attempts to enforce contractual or regulatory compliance on a product sponsor or an overseas manufacturer, with all of the attendant jurisdictional difficulties.

Conversely, it has been argued that reliance on a single, domestic fractionator may deny Australia access to the most recent advances in plasma product technology. The Review notes that avenues do exist for new, imported products displaying advanced clinical benefits to be made available to Australian patients, under the national blood arrangements, should clinical demand so justify. The fully subsidised supply of recombinant clotting factors, a measure adopted in 2004, is evidence of this capability under existing arrangements.

If a European-based fractionator were to be awarded a contract to fractionate all of Australia's plasma, there would be few, if any, concerns regarding safety, quality and efficacy of products, because all European manufacturers operate under the regulatory guidance of both the European Medicines Agency (EMEA) and a country-specific regulator. The standards that the TGA applies are derived from the same source as those applied in the European Union: Australia has adopted the standards contained in the British Pharmacopoeia, which in turn is harmonised with the European Pharmacopoeia.

In broad practical terms, there is no apparent reason why a European-based fractionator could not satisfy the TGA registration and certification requirements in respect of product safety, quality and efficacy, although changes to product presentation and plasma master files would be required.

Post-market surveillance of Good Manufacturing Practice (GMP) is potentially another matter. Under existing arrangements, the TGA has been able to certify fractionation plants that are undertaking or could undertake production of plasma derived products for Australian consumption. However, in circumstances where all Australian plasma, or a substantial proportion of it, were sent to Europe for fractionation, the need for closer inspection and audit by the TGA may arise. Certainly if Australia were willing to accept inspection and audit by European inspectorates in lieu of direct TGA surveillance, as occurs under existing Mutual Recognition Agreement (MRA) provisions, there should be no insurmountable problem. If for any reason, however, the TGA found it necessary to conduct its own inspections or audits, difficulties might arise.

The Review has been advised by the EMEA that joint inspections or accompanied inspections should be possible, given notice. Either arrangement would involve prior notice both to the EMEA and to the fractionator whose plant is to be inspected. Options for regulatory reform under a toll fractionation model are discussed in Chapter 8.

The situation in the United States is different again. In regard to plasma imported into the United States for fractionation and subsequent export as finished product, the US Food and Drug Administration (FDA) applies a regulatory regime different from that exercised for products marketed domestically. The main involvement of the FDA in respect of the fractionation of Australian plasma by a US fractionator would arise in the context of FDA inspections of US fractionation plants generally. It would be up to the TGA to conduct any product-specific inspections or audits in US plants, and provision to cover this eventuality could be included in any contract with a US-based fractionator.

All three of the options discussed in this chapter have the potential to provide assurance of the safety, quality and efficacy of plasma products manufactured for the Australian market. On balance, the Review Committee believes that Option One offers the TGA the most efficient alternative in terms of hands-on monitoring and surveillance of the fractionation of Australia's plasma. While the TGA has in place well-established arrangements, under MRAs, for ensuring regulatory equivalence in the certification, and auditing of GMP compliance, of overseas manufacturers, these arrangements could need review if Options Two or Three were implemented. As discussed in Chapter 8, in these circumstances there may be need for renegotiation of those provisions in the EC/EFTA MRAs that relate to the conduct of joint inspections and audits of manufacturers of high-risk products such as plasma products.

Yield

Yield, particularly for IVIg, is an important parameter and has been given close consideration by the Review. Improving IVIg yield narrows the gap between plasma collected and IVIg demanded. The higher the yield of IVIg, the more efficient is the use of plasma, a scarce and valuable resource.

Australia's high level of self-sufficiency in plasma products has been bolstered by the steadily increasing yields of IVIg delivered by the domestic fractionator. The most recent public indication of yield confirms a level of greater than 5.0 grams of IVIg per litre of starting plasma.[2] The current contract with CSL Limited specifies a minimum yield for IVIg, and CSL Bioplasma is currently performing well above that minimum specification.

At present levels, domestic yield is well in excess of the global industry average yield, which, according to unpublished and anecdotal data, is between 4.0 grams and 4.75 grams per litre. The only publicly available yield data comparable to that provided by CSL Limited is the yield rate reported for Norwegian plasma fractionated in Europe, which stands at approximately 4.2 grams of IVIg per litre.[3]

As IVIg yield rates increase, there is a corresponding lessening of pressure on plasma collection rates, because all plasma collected (except for that used for hyperimmune production and clinical purposes as fresh frozen plasma) is used for IVIg production. However, the rate of growth in IVIg demand in Australia has not been matched by a corresponding increase in the amount of plasma available for fractionation, even though the Australian Red Cross Blood Service has missed collection targets in only one year (2005–06).

2 See <http://www.csl.com.au/Investors.asp>: CSL Full-year Result Announcement for 2006, 23 August 2006.

3 B. G. Solheim, reported in a paper presentation and panel discussion at the 2006 Australia New Zealand Society for Blood Transfusion, Hobart, 15–18 October 2006.

Yield would be a determining factor in the award of any contract to an overseas fractionator. The benchmark against which yield would be adjudicated would be the yield for IVIg that was being achieved domestically at the time a new contract was under consideration.

On the basis of information provided to the Review, it appears unlikely that any other fractionator could match the IVIg yield currently being achieved by CSL Bioplasma. The CSL Bioplasma yield is known, whereas the yield rates of most other fractionators are either unknown or not supported by verifiable data. Those overseas fractionators that have lodged submissions to the Review have argued that yield data is highly commercially sensitive; however, although unwilling to provide this data for consideration during the Review process, they have advised that they would furnish yield rates as part of any tender for fractionation services for Australia.

Because of insufficient domestic plasma collections, Australia is already importing some IVIg manufactured from overseas-sourced plasma. Should an overseas toll fractionator realise a lower overall yield for IVIg than is being achieved under the current arrangements, there would be a net increase in the requirement for plasma.

Another aspect of yield that is of concern relates to the production of plasma derived Factor VIII. While many Factor VIII purification methods clear prions to a large extent,[4] the manufacturing process used by CSL to manufacture Biostate was judged by the Transmissible Spongiform Expert Advisory Committee (TSEAC) to result in a small residual risk.[5] The Therapeutic Goods Administration now requires, as an additional precautionary measure, that plasma used in the manufacture of this product be collected from donors who have not travelled outside Australia or New Zealand since 1 January 1980.

This measure has raised the concern that in future years there may be insufficient special plasma available for the domestic production of plasma derived Factor VIII. This is despite the fact that 85% of current demand for Factor VIII is being met by recombinant product.

A move to overseas fractionation would relieve this concern, because all overseas fractionators that have expressed an interest in fractionating Australian plasma use different technologies; should a contract be awarded to a manufacturer relying on other processes, the entire collection of Australian plasma would be available for the production of plasma derived Factor VIII.

In summary, on the criterion of yield, there is an apparent level of risk associated with resorting to overseas fractionation of Australian plasma, whether in whole or in part. Overseas fractionation may result in a reduction in the total amount of IVIg produced from Australian plasma, leading in turn to a greater reliance on IVIg manufactured from overseas-sourced plasma. On the other hand, overseas fractionation may remove the risk to supply sufficiency currently associated with plasma derived Factor VIII.

On balance, the supply of IVIg is considered to be of much greater consequence for Australia. Should supplies of domestically manufactured plasma derived Factor VIII prove to be insufficient in the future, it would be a relatively simple process to put in place as a contingency measure a standing offer arrangement for the supply of imported plasma derived Factor VIII.

4 T. Kriel, 'Industry TSE clearance studies for plasma-derived Factor VIII', presentation, September 2006. <http://www.fda.gov/ohrms/dockets/ac/06/slides/2006–4240S1_7_files/frame.htm>

5 S. Caris, 'New donor requirements for plasma derived Factor VIII in Australia', National Haemophilia, 153, March 2006, p 6. <http://www.haemophilia.org.au/sitebuilder/knowledge/files/254/nhno153march2006pg1-10.pdf>

It is not possible for the Review to forecast the competitive yields that may emerge during any future tender process, but the Review is mindful of the need to maintain the highest possible yields for all products fractionated from Australian plasma, and for IVIg in particular, if Australia's present level of self-sufficiency is to be maintained. On the evidence available to the Review, the IVIg yield being achieved by CSL Bioplasma would appear to be high when compared with that achieved in the fractionation sector generally.

Expenditure and value for money

The Review's terms of reference call for an assessment of options having regard to value for money and expenditure considerations. The ability of the Review to make such an assessment is constrained by the restricted nature of available information on the global plasma fractionation industry and the global market for plasma derived products. Similar shortcomings in the available data were noted by the Stephen Committee, which reported to government in 2001.

Unlike the related pharmaceutical industry, the fractionation sector is characterised by a heavy dependence on tenders and bipartite (and therefore confidential) procurement agreements. There are no published price lists or reliable sources of pricing intelligence to assist in the development of alternative value-for-money models.

Only one small organisation (Marketing Research Bureau Inc.) routinely surveys, and publishes global market reports on, the fractionation industry; even then, the authors of these reports qualify them as being based on information provided by companies and individuals rather than being drawn from material in the public domain. In the case of Australia, prices applicable under the Plasma Products Agreement with CSL are agreed only after protracted and intense negotiations conducted by the National Blood Authority on behalf of all Australian governments. This process is directed at achieving the best possible value for money given that international price comparisons are not readily available.

The absence of global pricing information means that opportunities for benchmarking are limited, and presently occur only when the NBA is able to obtain commercial-in-confidence information during its fact-finding missions or when a standing offer is negotiated for the contingency supply of a plasma product. These constraints notwithstanding, much of the NBA's activity to date has been directed towards achieving lower prices for plasma and recombinant products, and indeed this effort appears to have been conspicuously successful.

The Review notes that the Commonwealth Procurement Guidelines seek to encourage competition as an important component of achieving value for money. In respect of plasma products, Australia's existing contingency arrangements, which involve the negotiation of standing offers, do allow for some limited competitive elements to be introduced into the Australian market. These arrangements provide the opportunity for participation in the Australian market by those international fractionators that wish to compete for Australia's contingency supply business. To date, only one international fractionator has availed itself of the opportunity to compete for a market segment valued at A$24 million in 2006–07; this manufacturer has registered its products in Australia and has bid for standing offer status for its

products. There are opportunities for other international fractionators to follow this lead, given the indications that, for IVIg at least, the gap between domestic demand and supply will widen over time, thus making the contingent supply segment of the market more attractive.

It needs to be recognised that there would be substantial costs associated with a move to a toll fractionation arrangement in respect of Australian plasma, following a competitive procurement process. These additional costs would not be limited to those arising as a result of longer lines of supply or the greater level of risk to supply security. There would be an inescapable impost on an international fractionator (in terms of registration costs), just as there would be additional costs for the Australian government sector, arising from the need to build a larger National Reserve of products to compensate for a longer turnaround time between plasma collection and finished product delivery.

Ultimately all additional costs would be borne by the Australian taxpayer either in the form of product prices to compensate an overseas fractionator or by direct additional costs incurred by government agencies. It is estimated that an additional six months of inventory of finished products would be required overall, thereby detracting to that extent any potential benefit that may be achieved in terms of lower prices.

The cost to Australian governments of fractionation services provided by CSL Bioplasma is currently in the vicinity of A$400 per litre (excluding the cost of plasma). This figure includes the cost of manufacturing low-volume, high-value hyperimmune immunoglobulins. It is quite possible that a contested procurement process could lead prima facie to lower fractionation charges, notwithstanding the additional but marginal logistical costs involved in a toll fractionation arrangement.

However, as indicated previously, Australia could not escape substantial one-off costs if it moved to an arrangement whereby all Australian plasma was fractionated overseas. Any projected savings in terms of direct fractionation charges would need to be offset against these additional costs, as well as against national interest factors. There may also be recurrent additional costs for the acquisition of additional imported IVIg, should the yield achieved by an overseas manufacturer be lower than that currently being achieved by CSL Bioplasma.

Finally it should be noted that consideration of value for money cannot be restricted to consideration of price alone, but has to include assessment of intangibles related to the national interest. These include the need to maintain a domestic biotechnology capacity, the value of Australian infrastructure and investment, the engagement of Australian intellectual talent in an essential domestic industry, and the broader strategic value to the nation of a world-class domestic fractionation capacity.

Plant capacity

The current annual capacity of CSL Bioplasma is 500 000 litres of plasma. Australia's present requirement for fractionation capacity, which takes contractual and legislative precedence over any toll fractionation arrangements, stands at approximately 329 000 litres (2006–07), inclusive of hyperimmunes. This requirement is expected to double by year 2015–16.

CSL has indicated to the Review that the throughput capacity at the Broadmeadows plant can be increased to 750 000 litres annually through the introduction of additional equipment, within the existing infrastructure. A further expansion to 1 000 000 litres capacity is feasible at the existing Broadmeadows plant site but would require additional buildings and services.

Expanded capacities of this order would be sufficient to accommodate Australia's projected plasma collections out to year 2015–16, as well as a continuation of toll fractionation capacity for regional countries.

Of the seven overseas fractionators that have expressed interest in processing Australian plasma, three are considered to have the capacity to fractionate the entire Australian plasma collection. These are Baxter Healthcare, CSL Behring and Talecris. A further three, Bio Products Laboratory (BPL), Sanquin and Laboratoire Français du Fractionnement et des Biotechnologies (LFB), have limited spare capacity and would most likely not be candidates for the fractionation of the entire Australian plasma collection. Octapharma currently has a capacity of 1.8 million litres, spread across three plants, but has stated intentions of building capacity to 3.0 million litres and in these circumstances could probably accommodate all of Australia's fractionation requirements. All seven organisations would be capable of fractionating a share of the total Australian plasma pool.

Existing plant capacities are detailed in table 9.1.

Table 9.1 World's largest plasma fractionators

Fractionator	Commercial (C) or Not-for-profit (NFP)	Capacity - '000 litres	2005 Throughput - '000 litres	Utilisation (%)
CSL Limited (incl. CSL Bioplasma)	C	5950	5050	84.9
Talecris	C	4100	2710	66.1
Baxter	C	4000	3400	85.0
Grifols	C	3400	1768	52.0
Octapharma	C	1800	1600	88.9
Kedrion	C	1200	1050	87.5
Chengdu Inst.	C	800	350	43.8
Japan Red Cross	NFP	800	525	65.6
LFB	NFP	800	650	81.3
Shanghai Blood Inst.	NFP	800	600	75.0
BPL	NFP	750	400	53.3
Sanquin*	NFP	800	425	53.1

Source: Derived from Marketing Research Bureau data, 2006.

* If the proposed joint initiative between Sanquin and Biotest proceeds, the resultant entity would have a capacity of around 1 million litres, ranking it seventh on the list, by capacity (after Kedrion).

The Review's assessment of the plant capacity of those organisations that have expressed interest in the possibility of fractionating Australian plasma may be summarised as follows.

Table 9.2 Assessment of plant capacity of major fractionators

Fractionator	Capable of fractionating all Australian plasma	Capable of fractionating a share of Australian plasma	Comments
CSL Behring	yes	yes	Some question as to whether CSL Behring would compete against CSL Bioplasma. CSL Behring plants operate under a centres-of-excellence model.
Baxter Healthcare	yes	yes	Has indicated that capacity exists in Vienna plant complex.
Talecris	yes	yes	Currently no information on spare capacity but company has expressed interest. Production spread across two plants.
Octapharma	perhaps	yes	Plans to increase capacity to 3 million litres. Has three plants in Europe, each capable of producing entire Octapharma product range.
LFB	no	yes	LFB interested in fractionating a maximum of 100 000 litres of Australian plasma. Production spread across two plants.
BPL	no	yes	Participation in a tender would depend on outcome of current government review of operations.
Sanquin	perhaps	yes	May be capable of fractionating all Australian requirements, depending on outcome of Biotest joint venture negotiations. Production spread across two plants.
CSL Bioplasma	yes	yes	Current and future capacity sufficient to meet Australian needs. CSL Bioplasma operates under a tailored self-sufficiency model.

Source: Derived from information held by the Department of Health and Ageing.

Thus all of the above fractionators may be considered in terms of Option Three, but Option Two would probably result in a reduced field of four to five fractionators.

Product range

CSL Bioplasma currently produces a range of 13 individual plasma derived products in 21 different pack sizes and presentations, tailored to the requirements of Australian clinicians and end users. Even though this range does not represent the entire range of therapeutic agents that can theoretically be produced from human plasma, it does represent one of the more extensive ranges to be found among the various fractionators. The products that are not manufactured domestically (such as Factor XI and Factor XIII) are those that are not economically viable or those that are yet to reach domestic demand levels that would justify domestic production (e.g. protein C or alpha-1 antitrypsin).

Included in the current domestic product range are six low-volume, high-value products made from special plasma and described as hyperimmunes. With the possible exception of Rh(D) immunoglobulin, it may be difficult to secure overseas fractionation of hyperimmune products using Australian plasma, because of the very low volumes involved. The domestic fractionator currently manufactures these low-volume products using a small-scale dedicated Cohn fractionation plant at Broadmeadows.

The research and development activities of the CSL Group are centred in Melbourne, at the Parkville and Broadmeadows sites but principally the former. Australia is therefore well placed to benefit from new or improved products that are researched and developed in Australia for the global markets.

One of the issues confronting the Review has been the fact that none of the overseas fractionators that have expressed an interest in the possibility of fractionating Australian plasma currently have a product range that directly matches that currently required by Australian clinicians and end users.

Table 9.3 compares the current Australian domestic product range with the current suites of products made by international fractionators.

In each case where there is a gap, one of two events would need to occur if Australia's requirements were to be fully met by a single overseas fractionator. Either the successful fractionator would need, as a prerequisite to contract implementation, to develop and register the missing products in the range – a process that could take up to two years, with no guarantee of the fractionator being awarded the contract. Alternatively, the Australian Health Ministers' Conference could deem the missing product(s) as being of marginal importance and agree to acquire them on the open global market (as is currently the case with a number of very low-volume products). The latter alternative would necessarily involve a dilution of Australia's preference to use domestic plasma wherever possible.

It is essential to note that even though an overseas fractionator may presently manufacture a given product type, this does not mean that the product is available in the strength, concentration or pack size used in the Australian clinical setting. It is not just a matter of adjusting the strength of a product to suit Australian requirements. A new formulation will require substantial additional development and clinical trial work in order to demonstrate safety, quality and efficacy prior to registration of the reformulated product on the Australian Register of Therapeutic Goods (ARTG). A current example is imported IVIg. Under contingency

Table 9.3 Manufacturers and products

	CSL Bioplasma	CSL Behring	Baxter	Octapharma	Sanquin	LFB	Talecris	BPL
Albumin	registered	produces	produces	produces	produces	produces	produces	produces
IVIg (liquid)	registered	produces	produces	registered	produces		produces	produces
IMIg	registered	produces			produces			
CMV immunoglobulin	registered							
Hepatitis B immunoglobulin	registered				produces	produces	produces	produces
Rh(D) immunoglobulin	registered		produces	produces	produces	produces		produces
Tetanus immunoglobulin	registered		produces		produces	produces	produces	produces
Zoster immunoglobulin	registered				produces			produces
Plasma derived Factor VIII	registered	produces	produces	registered		produces		produces
Plasma derived Factor IX	registered	produces	produces	produces	produces	produces		produces
Antithrombin	registered		produces	produces		produces	produces	produces
Prothrombin complex	registered		produces	produces	produces	produces		produces

Source: Adapted from information held by the Department of Health and Ageing.

arrangements, there are a variety of strengths, pack sizes and presentations for clinicians and other health professionals to deal with.

The Review has received representations that seek to limit, as far as possible, the variety of strengths, pack sizes and delivery methods appearing in the clinical environment. It is highly likely that the National Blood Authority would, when issuing a Request for Tender, specify strength, pack size, form of presentation and number of different pack sizes, according to established domestic market needs and preferences in order to restrict the impact on clinicians and recipients as a result of any prospective change of manufacturer. It is also likely that the Therapeutic Goods Administration would require labelling, package inserts and prescribing monographs to be in a form adapted specifically to Australian requirements. A successful tenderer would need to have demonstrated, as a prerequisite to contract implementation, compliance in regard to all of these requirements.

Even though a number of fractionators currently manufacture some of the low-volume products (particularly hyperimmunes), there is no guarantee that a successful tenderer would necessarily consider the production of such products from Australian plasma to be an economic proposition. In the case of at least one product, Rh(D) immunoglobulin, the continued use of Australian plasma would be considered as being essential and this would raise questions for at least one fractionator that does not include this product in its existing product range.

Fractionators use different operating models that are designed to maximise particular efficiency goals in production. CSL Behring, for example, uses a 'centres of excellence' model, whereby each of three plants specialises in the production of one group of products. CSL Bioplasma is not part of the 'centres of excellence' model but remains a 'stand-alone' fractionator using predominantly chromatography technology (except for hyperimmune production) to produce a product range specifically tailored to Australian clinical requirements.

On the criterion of product range, it follows that what Option One offers is superior in terms of supplying Australia's specific needs in the foreseeable future. Option Two, and to a lesser extent Option Three, would require prospective tenderers to have developed and registered a range of products that meet Australian specifications prior to the implementation of any contract. These options could involve substantial expense for interested tenderers, thereby prospectively limiting the number of tenderers to those that are prepared to accept the financial risks involved.

Product registration

Under Option One, the plasma derived products required by the Australian community are already registered under the Australian Register of Therapeutic Goods. However, registration, while being an essential prerequisite in most cases, does not translate into automatic listing under the national blood arrangements. These arrangements anticipate that only one domestically produced or imported brand of each product type will be supplied free of charge to end users. The exception is where domestic supplies of a product type are insufficient to meet total demand, in which case a second imported brand may be added to the list as a contingency.

These arrangements limit the number of registrations that the Therapeutic Goods Administration is required to process in order to provide for Australia's plasma product demands. Should the provision of fractionation services in respect of Australian plasma be opened to competition, the TGA would need to cope with multiple applications for registration of each product type as a prerequisite to contract implementation by a chosen manufacturer.

While the direct costs of registration are fully recoverable from manufacturers, there would still be timing and capacity questions for the TGA in respect of the provision of sufficient trained scientific staff and adequate resources to carry out the registration and subsequent regulatory processes. Cost recovery alone might not offset the additional structural and resource demands to be borne by the TGA in this case, and the additional financial burden would ultimately fall on the Australian taxpayer.

Prior to the commencement of a contract arising from a Request for Tender process for the fractionation of all of Australia's plasma, intending overseas participants in the process would need to ensure that the candidate products have been included on the ARTG. All candidate products, regardless of whether registered in Australia or not, would require some level of registration or re-registration depending on how closely the products conform to Australian requirements in terms of strength, pack size, presentation and route of administration and plasma source.

Essentially this could mean that all candidate products will be subjected to a full registration process because the only imported products already registered in Australia that would prospectively be manufactured from Australian plasma are of differing strengths and volumes and employ differing methods of administration compared with the equivalent domestically produced products. Presumably, the intent of the competitive process would be to simply replace the domestically produced products with direct equivalents manufactured by an alternative fractionator.

At the very least, a candidate product will need to have a revised Plasma Master File submitted (based on Australian plasma) and that will take between three and six months to achieve upgraded registration status following lodgement. All other candidate products would need to be the subject of a full dossier submission, which will take at least 18 months to process for inclusion in the ARTG following receipt of dossiers.

In the case of an open tender for the fractionation of all of Australia's plasma collection, this could mean a registration workload for the TGA amounting to as many as 60 or more additional candidate products, although it is doubtful that some manufacturers would commit to this degree of expense as a prerequisite to the award of a contract.

One measure of the reluctance of some overseas fractionators to commit to registrations prior to the announcement of a contract can be seen in the small number of the same fractionators who sought to register product and participate in the IVIg contingency supply standing offer, a market segment valued at A$24 million in 2006–07.

There is no doubt that a move to Option Two or Option Three would involve the TGA in a substantial additional workload in terms of new product registrations. Such a move would also involve the TGA in more extensive GMP surveillance and audit operations at overseas sites post product registration. On this basis, Option One must be preferred.

Market share and competitiveness

The overall market for plasma derived and related products in Australia is now split among CSL Bioplasma, which fractionates all Australian plasma, and the overseas suppliers that provide all other products, including both fractionated and recombinant forms. In value terms, the split is approximately 50:50.

CSL Bioplasma enjoys an overwhelming majority share of the IVIg market segment and the totality of the albumin market segment but has lost most of the clotting factor business to imported recombinants, predominantly supplied by Baxter and to a lesser extent by Wyeth and Novo Nordisk.

In the case of IVIg, there has been some erosion of the domestic fractionator's market share, due to the importation of a competing brand product arising from the shortfall in domestic plasma collections. These imports provide some element of competition in respect of the largest segment of the plasma products market.

Legislative issues

Provisions in the CSL Act constrain CSL in respect of the operations of the CSL Bioplasma plant at Broadmeadows. These national interest provisions were included in the legislation when CSL was privatised, in order to secure the domestic supply of plasma derived products for the Australian community. Should Option One continue, these provisions will remain in place and will serve to ensure that Australia continues to enjoy the security of an onshore fractionation facility.

Alternatively, if either Option Two or Option Three were to be implemented, there would need to be a review of legislative provisions so as to ensure that CSL Bioplasma could compete with other fractionators on an equal footing. This process could involve significant amendment to the CSL Act and other legislation.

The Review is of the opinion that for security of supply reasons, maintenance of the provisions of the CSL Act should continue. This would be consistent with a preference for Option One and is also consistent with the Commonwealth Procurement Guidelines currently in force.

Domestic industry and research

The Review has received strong representations from the Government of the State of Victoria, supported by the Government of the State of South Australia, in favour of maintaining the existing domestic facility as the dedicated national fractionator of Australian plasma.

The continued presence in Australia of the CSL headquarters, and of the research and development operations of CSL Limited, cannot be separated from the continued existence in Australia of CSL Bioplasma. The loss of CSL Bioplasma would have major implications for the biotechnology sector in Australia, including for research and collaboration opportunities between industry and the tertiary education and research sector in Australia.

CSL's research and development effort in Victoria has provided and continues to provide substantial benefits in the form of major new products, such as Gardasil®, the first vaccine against cervical cancer, and products essential to Australia, such as other vaccines and anti venoms specific to Australia's needs. CSL in Australia provides one of four World Health Organization centres collaborating in influenza control and is the only such centre in the Southern Hemisphere.

CSL Limited is the Australian Government's partner of choice to provide influenza vaccine to protect Australians, both during the annual flu season and in the event of an influenza pandemic; CSL is currently working closely with the government to accelerate its prototype pandemic influenza vaccine clinical trial program based on the H5N1 avian virus. CSL has helped ensure that Australia has one of the largest antiviral stockpiles per capita in the world. By early 2007, Australia will have enough antivirals to provide coverage for nearly 44% of the Australian population.[6]

Regional relationships

Under Option One there would be no disruption to fractionation operations at the domestic fractionation plant. New Zealand, Malaysia, Singapore and Hong Kong would be free to continue existing toll fractionation arrangements should they be required.

6 <http://www.health.gov.au/internet/wcms/publishing.nsf/Content/phd-health-emergency-qanda.htm>.

Two of these governments have lodged submissions supportive of a continuation of operations at Broadmeadows and have indicated that each would experience difficulty in economically replacing toll fractionation services currently provided by the Broadmeadows plant. Another government has indicated its reliance on CSL over many years and confirms that this is likely to continue.

In each case, the annual volume of regional toll fractionation arrangements is low (maximum 38 000 litres annually), which implies difficulty in attracting interest from large-scale fractionators.

New Zealand in particular has indicated to the Review that it is content with the current toll fractionation arrangements and has indicated that there would be substantial disadvantage for New Zealand should that arrangement cease.

The ability of the domestic fractionator to continue to offer toll fractionation facilities to regional countries depends on the ability to meet domestic Australian requirements as a first priority. If the Australian business diminished significantly, then it follows that the plant may no longer be in a position to offer fractionation services to regional countries.

Option One has the advantage of preserving the current constructive regional relationships.

Contract duration

The duration of a contract to fractionate Australian plasma overseas would need to be determined having regard to a range of factors that do not necessarily apply in the case of existing arrangements. These include:

- exchange risks
- plant capacities
- competing priorities
- product ranges
- international transport costs.

A short-term contract may be preferred for exchange risk reasons, even if the contract provides for Australian currency to be specified. The Department of Finance and Administration advises that the provisions of Financial Management Guidance #2 indicate that the Australian Government has a policy that its entities should not engage in direct or indirect hedging of foreign exchange risks. One form of indirect hedging is through specifying fixed prices in Australian dollars. Instead, as a general principle, unless exceptional circumstances apply, price provisions should allow for variation according to movements in exchange rates between Australia and other countries.

An overseas fractionator may not wish to commit to priority fractionation of Australian plasma if existing plant capacity is tight and market demands and opportunities are volatile. A fractionator may wish to maintain flexibility through a short-term contract in order to be better placed to accept new and more attractive assignments.

The product mix of a fractionator may be in the process of change (for example, to focus on recombinants), in which case the fractionator may not wish to be locked into a longer-term contract involving fractionation products. Given the uncertainty of global oil prices and the knock-on effects on freight rates, a fractionator may not wish to extend exposure to additional freight costs over the longer term.

Conversely, it would be in the interests of Australia not to indulge in a short-term contract when this implies a potential future change in product brand and even product characteristics. The cost of contracting is high for both the client and the supplier alike. One or both parties may prefer a longer contract period in order to lessen the costs of contract renewal.

In considering duration of contract, the nature of toll fractionation needs to be borne in mind. While Australia may be seeking to ensure supply continuity through priority provisions in a contract, the fractionator will in all likelihood be quoting on the basis of marginal rather than full pricing in order to fill short-term unused capacity. Being locked into a marginally priced contract over a significant period of time may be seen to deny the fractionator the opportunity to secure alternative business at a higher rate of return.

On the whole, however, issues of duration arise in respect of all three options and are not the most critical factors in a judgement about the merits of each option.

Contract enforcement

The existing Plasma Products Agreement between the National Blood Authority (on behalf of all Australian governments) and CSL Limited (on behalf of CSL Bioplasma) is a contract drawn for the benefit of Australian parties operating in an Australian environment. Contractual obligations on both parties are therefore adapted to particular domestic needs of the parties and include remedies that may be readily applied in circumstances of default.

A contract to secure the overseas fractionation of Australian plasma would be a much more complex instrument. As a first principle, it would be desirable to be able to ensure that the contract would be capable of enforcement for specific performance not only in Australia but also in the country where the fractionation takes place. Clearly this presents major problems of legal jurisdiction. In turn, it limits the extent of sanctions that can effectively be applied in an overseas context; that is, both legally and practically.

For example, under the PPA, the NBA enjoys 'step-in' rights in the event that CSL fails to meet specific contractual obligations. In the case of an overseas fractionator, contractual 'step-in' rights would seem superfluous. This is because an overseas fractionator would be highly unlikely to agree to such a stipulation in the first place and, even if it did, the practical difficulties of 'stepping-in' under an overseas jurisdiction would render such a provision of doubtful value.

The best guarantees of performance that could be expected would arise from a tripartite agreement between the NBA, the Australian sponsor of the registered products (preferably a corporate subsidiary of the overseas fractionator) and the overseas fractionator.

While the practical difficulties of enforcement in the case of the fractionator in an overseas jurisdiction would exist, some level of comfort could be afforded by an irrevocable bank guarantee against specific performance. This may provide some level of monetary compensation, but it does nothing to secure or restore the critical flow of finished products derived from Australian plasma. The domestic sponsor would of course be exposed to the full force of the applicable state or territory law.

The degree to which contractual limitations exist when an overseas-based fractionator is involved is a matter for consideration in deciding whether a contract to fractionate all or part of Australia's plasma overseas is a viable and acceptable option. A failure to perform for whatever reason could place at risk Australia's supply of life-preserving plasma derived therapeutics.

The relevant contract or performance guarantee should therefore specify that the governing law is that of the state or territory in which the Commonwealth agency is located and that the parties submit to the jurisdiction of the relevant state or territory courts. Nevertheless, even if the Commonwealth were successful in obtaining a judgement from an Australian court against an overseas fractionator, it would be difficult to enforce that order overseas, particularly in the United States. Enforcement of judgements overseas (where this can be done) is usually a costly and protracted process.

Product liability

Product liability is already a complex area of law; the possibility of exporting Australian plasma for processing at an overseas location adds another dimension to product liability that has not previously been encountered in the Australian blood sector. In its report on actuarial, demographic and insurance issues to the Review, the Allen Consulting Group observed:

> There has been only one HIV infected transfusion of blood since screening commenced in 1985 and no Hepatitis C infected transfusions in Australia in the last five years. There have been three cases of variant CJD transmission, associated with non-leuco-depleted red cell transfusions in the UK, but no transmissions reported for plasma products.
>
> ARCBS estimates of probabilities of transmission of viral infections in transfusions subject to HIV antibody testing and Nucleic Acid Testing (NAT) are one in 7,299,000 and the probabilities of transmission of viral infections in transfusions subject to HCV antibody testing and NAT are one in 3,636,000 based on data from July 2000 to June 2003. The risks for plasma products are lower again.
>
> The liability costs associated with a single case of infectious product may be extremely high, but the probability is extremely low, producing a moderate risk cost. For example, a new virus may infect several hundred people before being discovered, at a cost of hundreds of millions of dollars. However, given the viral testing and inactivation processes in place, the probability is extremely low. Overall we have assumed an annual risk cost of 0.5% of production based on a one in a hundred year event and a cost of $200 million.

The Australian community is no stranger to international product liability processes. A number of class actions involving claims against international suppliers are a matter of record. It is noteworthy that a very high proportion of Australia's pharmaceutical product needs are manufactured overseas. The fractionation of Australian plasma overseas represents just another opportunity among many for issues of product liability to arise. In the circumstances, overseas fractionation would not present problems in terms of product liability that are different from those affecting pharmaceutical products generally. Nevertheless, there are still potential difficulties in bringing actions in the event of a claim for negligence arising.

Summary of options

Option One

Under this option, CSL Bioplasma would continue to receive plasma for fractionation from the Australian Red Cross Blood Service and would maintain the present product range, with new additions where appropriate (e.g. subcutaneous immunoglobulin and an improved product range). A perceived disadvantage of Option One is that it is not an internationally competitive procurement option but instead represents a continuation of sourcing from a single preferred supplier.

On the other hand, there would be some very substantial advantages. The Therapeutic Goods Administration would retain its ability to directly regulate the domestic fractionator and to apply sanctions as circumstances may dictate. There would be no need to modify existing negotiations and MRAs that serve to provide the Australian community with a high level of guarantee in respect of the safety and continued supply of essential fractionation products. The need to register multiple brands of product in order to facilitate an open tender process would be obviated.

CSL as the domestic fractionator would continue to maintain its global research activities in Melbourne, thus enabling ongoing collaborative research with Australia's tertiary institutions. CSL's research and production effort would also serve to maintain a critical mass of biotechnology expertise in Australia as opposed to the export of this capacity to the Northern Hemisphere, together with the accompanying loss of intellectual capital.

In view of the prospective supply and demand situation, the National Blood Authority would be able to effectively benchmark prices for at least one major product (IVIg) through the operations of standing offer arrangements already in place. At the same time, overseas fractionators would be able to participate in the Australian market for plasma derived and related products through the various procurement arrangements, including standing offers, undertaken by the NBA.

The domestic fractionator would continue to be in a position to offer toll fractionation services to regional countries.

Option Two

While overseas fractionation is potentially achievable in a technical sense, Australia could not move to a situation involving the overseas fractionation of all of Australia's plasma collection without making a number of compromises on important issues of principle and policy.

The domestic fractionation plant at Broadmeadows in Victoria is a national strategic asset. This plant employs 500 staff, including many with tertiary training in biotechnology. It is currently the largest fractionation plant in the Southern Hemisphere and provides fractionation services not only for Australia but also for other countries in the region

The loss of the contract for the fractionation of Australian plasma would almost certainly signal the closure of this plant and this would have wide ramifications, including a loss of domestic production, the loss of export markets and an increase in imports, and, potentially, an increase in Australia's trade deficit. Broadmeadows is a facility that was designed and built to service the Australian market. It does not compete internationally, apart from providing toll fractionation services for small markets in the region. Moreover, the plant is an integral part of CSL's total operations in Victoria and from a research perspective is integrally linked to CSL's operations at Parkville.

No substantial alternative fractionator currently manufactures the entire range of products presently sourced from the domestic fractionator. It also needs to be recognised that the economic basis for the maintenance of the blood and blood products supply in Australia (the national blood arrangements) is provided not only by the Commonwealth Government but also by the various state and territory governments. It is doubtful whether any state or territory government would accept Option Two. It is also certain that several would strongly oppose this option as well as Option Three.

A move to open competition would be inviting concerted opposition from the Australian public as is evidenced by the numerous submissions received and considered by the Review. It is an inescapable fact that the blood supply in Australia depends on a high degree of public confidence in the system, and any erosion of that confidence, for whatever reason, would be to the detriment of Australia and the Australian community.

Option Three

Of the three scenarios presented, Option Three would be the most complex to manage in terms of administration and logistics. It has the potential to provide an additional limited element of competition.

In terms of overall value for Australia, Option Three appears to offer only limited advantages but still suffers from most of the disadvantages of Option Two, with the additional disadvantage of significant administrative and management complexity.

The Victorian Government, supported by the Government of South Australia, has made strong representations to the Review that maintenance of the current arrangements is in the national interest of Australia. The submissions cite the need to maintain an onshore fractionation capacity in Australia and the need to retain Australia's leading biotechnology industry in Australia for the benefit of Australians.

The Victorian Government has indicated that the loss of CSL Bioplasma as the national fractionator could have serious implications for the biotechnology sector in Australia and for research and collaboration opportunities between industry and the

tertiary education and research sector in this country. The Victorian Government, supported by the South Australian Government, identifies the need to sustain employment opportunities for a growing cadre of tertiary-qualified workers in biotechnology. Both governments note also the level of security afforded the Australian community against adverse international events through the maintenance of CSL Bioplasma's onshore operations.

The views expressed by the governments of these two states are supported by the preponderance of submissions received by the Review from a wide range of Australian stakeholders representing consumer, clinical, academic and industry viewpoints.

A major concern arising out of Option Three is the likelihood that a split of plasma resources between a number of fractionators, while providing a means of benchmarking prices, may ultimately result in the discontinuation of fractionation activities at Broadmeadows. Once ceased, it would be highly unlikely that operations at the domestic fractionation site could be recommenced at some future date.

The Review has received strong representations to indicate that, if fractionation of Australian plasma were to take place overseas, then this could result in a substantial fall-off in the numbers of Australian volunteers willing to donate blood and plasma. Such a development would be contrary to Australia's policy of seeking self-sufficiency in blood and blood products. The Australian Red Cross Blood Service cites an unpublished survey of donors that indicates a strong preference for the retention of the current onshore fractionation arrangements. The survey suggests that significant numbers of donors would view adversely the possibility of their 'gift' being sent for processing overseas. While such research is not conclusive, the implied threat for Australia's blood and plasma supplies has to be taken seriously.

Submissions received by the Review leave little doubt that the Australian community at all levels does not support the concept of moving to open competition for the fractionation of Australian plasma. In some cases, the opinions expressed are based on a perceived increased level of risk of contamination if Australian plasma is sent overseas. Even though some of these opinions may not be well founded from a technical point of view, they are genuine and strongly felt concerns.

Of all the domestic concerns identified during the Review process, public confidence in the Australian blood supply is of paramount importance. Without in any way seeking to impugn the safety of the blood supply in other countries, the Review perceives that all sectors of the Australian community strongly prefer a closed system whereby blood and plasma are collected in Australia, plasma products are processed in Australia, and these products are provided for the benefit of Australians.

The overwhelming majority of submissions received by the Review consider that reliance on overseas fractionation, given Australia's remoteness from Northern Hemisphere fractionation sites, is a risk not worth taking. Open and unrestricted global markets for plasma derived products is not a view that would be supported by the weight of public opinion in Australia as evidenced by submissions to the Review.