# Executive summary

This is the first and final report of the Review of Australia's Plasma Fractionation Arrangements.

The Review has involved a comprehensive analysis of Australia's current arrangements for the collection of blood plasma from Australian donors and for the separation of this plasma as the basis for a range of therapeutic products designated for use within the Australian health care system.

## Global context

The global plasma fractionation industry, together with individual countries' national arrangements for the supply of blood and blood products to meet domestic need, contributes very significantly to the health care of many millions of people around the world.

The value of the global market for plasma derived products, together with alternative products manufactured via recombinant DNA technology, is currently assessed at approximately US$10.5 billion. The world market for plasma products grew by 5% between 2003 and 2005 and is forecast to expand by a further 11.5% in the period 2005–08.

The past two decades have seen dramatic changes within the global industry, the result primarily of mergers and acquisitions, the development of recombinant alternatives for existing plasma products, and increasing levels of regulation with respect to product safety.

The United States is the only country in the world that is totally self-sufficient in whole blood and in the full range of plasma products. Some 70% of the plasma collected globally is collected in the United States. In other countries, arrangements for the collection of plasma, and for its subsequent fractionation, reflect domestic demand together with various economic, demographic and historical factors.

Over the decade 2006–16, global demand for intravenous immunoglobulin (IVIg), commercially the most important of the plasma derivatives, is expected to increase by 65%. Additional clinical uses for IVIg, changes in clinical practice, or entry by the product into new markets, could generate even greater demand. Projections suggest that worldwide demand for albumin, another key plasma product, will experience more modest growth over the same period, increasing by 15%.

## Australia's arrangements

Australia's national arrangements with respect to the supply of fresh blood and of fractionated plasma products are unique and are not replicated in any other country.

Crucial to these arrangements is the contribution made by Australian donors. The many individuals who voluntarily donate blood or plasma on an ongoing basis

contribute a gift of immeasurable value to the health and wellbeing of their fellow Australians. Indeed it is difficult to conceive of a more altruistic form of community service than the regular donating of blood or plasma – where the gift may well be that of life itself. Over 400 000 people in Australia receive a blood product each year, and it is estimated that more than 50% of Australians will require blood or a blood product during their lifetime.

Also playing a vital role in Australia's arrangements for the supply of plasma derived products is the Australian Red Cross Blood Service (ARCBS), an operating division of the Australian Red Cross Society. The ARCBS is currently responsible for all collections of Australian blood and plasma, with plasma being sourced both from whole blood donations (recovered plasma) and from donors directly, via the process of plasmapheresis (source plasma). In its capacity as a humanitarian organisation of long and distinguished standing, the Australian Red Cross is held in high regard by Australians, and the association between the ARCBS and the national blood supply system is therefore likely to engender donor confidence, and confidence within the broader community, for years to come.

Plasma collected by the ARCBS from Australian donors is fractionated by CSL Bioplasma, a business unit of CSL Limited, at its plant at Broadmeadows, Victoria. Founded in 1916 as the Commonwealth Serum Laboratories, CSL has played a major role in the delivery of health care for nearly a century. In addition to fractionating Australia's plasma supply, CSL conducts leading-edge medical research and has for many years produced vaccines and other pharmaceutical products in quantities sufficient to enable Australia's health system to respond quickly and effectively to emerging public health crises. CSL's Broadmeadows plant is the only facility of its kind in Australia with the technology and expertise necessary for the efficient fractionation of the quantities of plasma collected by the ARCBS from Australian donors.

The National Blood Authority (NBA), a federal agency, manages the national blood supply system on behalf of Australian governments, monitoring demand for blood and blood products, managing procurement arrangements with product suppliers, and undertaking annual supply planning and budgeting. In its short period of existence the NBA has been conspicuously successful in ensuring greater value for governments.

The strong regulatory environment within which plasma products are manufactured and distributed in Australia is managed and monitored by the Therapeutic Goods Administration (TGA), an arm of the Commonwealth Department of Health and Ageing, to ensure that plasma derivatives are subject to the highest standards of regulation applicable to therapeutic goods.

The close oversight of CSL Bioplasma in its capacity as Australia's national fractionator, and of the ARCBS as the agency charged with collecting blood and plasma nationwide – together with the longstanding commitment by both organisations to health care in Australia, and the exceptional generosity of Australia's many voluntary blood and plasma donors – are the factors that combine to create the unique, world-class system that today governs the supply of plasma products to the Australian community.

The total cost of funding Australia's national blood arrangements for 2006–07 is estimated at A$650.7 million.

## Australian demand, present and future

While the great majority of plasma products provided to the Australian community are manufactured in Australia, from domestically sourced plasma, the importance of ensuring a secure and adequate supply of plasma derivatives, sufficient to meet the needs of all Australian patients, currently necessitates arrangements for the importation of some fractionated products.

Importation becomes necessary where clinical demand exceeds the quantities of a particular product that can be produced within Australia from available Australian plasma, or where a required product is low-volume and is not manufactured from available Australian plasma by CSL Bioplasma. All suppliers of plasma products for use in Australia operate under agreements that ensure security of supply, as well as reserve stockholdings.

The critical factor in forecasts concerning future demand for plasma products in Australia is the projected demand for intravenous immunoglobulin (IVIg). Over the past decade, demand for IVIg in Australia has been increasing at an annual rate of 14%, a growth rate much steeper than that for the supply of starting plasma available for fractionation. Since 2003–04, therefore, in order to meet the needs of Australian patients, the domestic IVIg supply has been supplemented with imported IVIg products.

Forecasts provided to the Review indicate that by 2015–16 the level of demand for IVIg in Australia will be between 2985 and 3687 kilograms of product per annum. The average of these two figures, 3336 kilograms, represents more than double the amount of IVIg currently being issued.

At present rates of product yield, this increase in demand for IVIg would mean that the amount of raw plasma collected from Australian donors in ten years' time must be more than double the amount of plasma collected today. If the forecast provided to the Review by the Allen Consulting Group (ACG) proves accurate (the ACG forecast anticipates a 7.7% annual growth in demand for IVIg), Australia will require 686 tonnes of starting plasma in 2015–16, compared with 308 tonnes in 2005–06, an increase of 123% for the decade.

It is clear, therefore, that a key issue – perhaps *the* key issue – in relation to Australia's current plasma fractionation arrangements is that the volume of plasma collected in this country must greatly increase if future demand for plasma derivatives, especially IVIg, is to be met primarily by products fractionated from Australian plasma.

While Australia has never been totally self-sufficient in respect of all plasma products, the Review is of the opinion that Australia should be as self-sufficient as possible and that self-sufficiency should remain an important national objective.

Donation trends to date, however, do not offer any certainty that Australia's donor pool can be increased to the levels necessary for providing the quantity of domestic plasma needed in order to meet projected demand.

## Assessment of alternative fractionation arrangements

The Review has closely examined fractionation arrangements in the United States and in Europe, and has given close consideration to possible alternative arrangements for Australia.

The Review has determined that if Australian plasma were to be fractionated overseas, rather than at a locally based fractionation plant, there would be a need for substantial initial

expenditure, extensive transitional planning, contingency plans, risk mitigation plans, and investment associated with registration and other compliance and approval processes.

There would also be significant additional ongoing costs associated with the overseas manufacture of plasma products for use in Australia. Some of these costs (e.g. for the transportation of Australian plasma to an overseas fractionation facility; for the return of finished plasma products to Australia; and for cold storage and warehousing) would be borne by the offshore fractionator and would be reflected in its pricing structures.

Major costs arising from the offshore fractionation of all Australian plasma would include a one-off 'transition cost', of approximately A$75 million. This would enable either the collection (if feasible) of sufficient additional domestic plasma to cover the 60-day withholding period if required (and the period required for sea transport) and scheduled processing time, or the one-off purchase of the same quantity of imported finished product. The National Reserve would thus have to be increased by an additional six months' stockholding, over and above the present inventory target of three months' supply of plasma products.

Moreover, on the basis that an offshore fractionator's yield of IVIg would most likely be less than the yield realised by CSL Bioplasma, projections indicate that overseas fractionation could result in additional annual purchasing costs for starting plasma.

It is also evident that overseas fractionation would see a doubling in lead time 'vein to vein' (i.e. the period that elapses between a donation of plasma and its clinical use, in the form of a finished plasma product).

Finally, there are potentially major risks associated with the offshore fractionation of Australian plasma. Although the scenarios envisaged carry a low probability of occurrence, their consequences would be costly and highly disruptive. For example, the loss of a 20-foot reefer container of plasma would mean a serious interruption to the supply of plasma products in Australia and would necessitate the acquisition of a compensatory quantity of overseas-sourced plasma, or of the equivalent in finished products fractionated from overseas-sourced plasma.

## Community expectations

Across the broad range of local submissions received by the Review, concern about the possibility of change to Australia's current blood arrangements was almost universal. Maintaining the existing integrity of these arrangements, together with the reliability and high levels of safety that they represent, is seen by the majority of stakeholders to be of vital importance.

Another key issue in terms of community expectations is that CSL Limited's Broadmeadows and Parkville plants are widely regarded as iconic establishments within the biotechnology sector, not only in terms of technology and R&D, but also of the employment opportunities offered by both facilities.

## Key conclusions

- If Australia is to be self-sufficient in the plasma required for the production of IVIg, then, given projected demand over the next ten years, a dramatic increase in domestic plasma collections by the Australian Red Cross Blood Service will be necessary. Achieving this increase will require of all Australian governments vigorous review and reform of current domestic plasma collection arrangements.

- In any event, Australia will need to maintain imports of plasma derived product in order to meet domestic demand. If the increases in plasma collections projected by the ARCBS are not met, then the requirements for imported products will increase considerably.
- Overseas fractionation of Australian plasma would involve significant transitional costs and, because of yield considerations, there would be the potential for an ongoing shortfall in the supply of IVIg and other plasma derived products. The consequent need to source these products via imports would have implications for the national self-sufficiency policy.
- There are potential supply chain risks involved in overseas fractionation of Australian plasma. While some of the risk scenarios are of low probability, their consequences would be expensive and disruptive. Addressing these risks would require either an impost on the National Reserve of plasma products or an added call on existing standing offers for imported product.
- Any supply to Australia of plasma products from overseas fractionators would require significant lead times and investment in registration and other approval processes. If registration of products were to be a prerequisite to tendering for the supply of plasma products to Australia, not all overseas fractionators would be likely to want to incur the costs of registration in the absence of a supply contract. If, on the other hand, product registration were to be required only after a tender contract had been agreed, then a lead time of at least two years would be needed for registration and approval processes.
- When the transitional costs, the risks, and the indeterminate yield ratios of overseas fractionation are considered against the national self-sufficiency objective, and when account is taken of the national strategic importance of CSL's plant at Broadmeadows, then overseas fractionation of Australian plasma is not an advantageous option for Australia.

## Recommendations

1. Ministers should note the Review's conclusion that overseas fractionation of Australian plasma is not an advantageous option for Australia. Ministers should also note the substantial regulatory and other changes, as set out in this report, that would be necessary in the event it were desired to alter present arrangements and invite overseas manufacturers to tender for the fractionation of Australian plasma.
2. In view of the prospect of substantial shortfalls between projected demand for plasma products in Australia, and domestic plasma collected by the Australian Red Cross Blood Service, urgent action must be taken to increase plasma collection rates. There needs to be a vigorous and creative campaign, led by Commonwealth, state and territory governments, to energise the community in favour of blood donation.
3. The Commonwealth, state and territory governments should safeguard the security of supply of plasma products for Australians by importing plasma products to address any shortfall and risks in supply of domestically manufactured products. Procurement of imported plasma products should be undertaken by an international competitive tender process, which could include provision for tiered pricing related to the volume of specific products required. This may also facilitate benchmarking by the National Blood Authority of domestically manufactured plasma products against prices for imported plasma products, in order to further the objective of value for money in future contract negotiations, consistent with other policies. Existing contracting, risk management and mitigation strategies for Australia's plasma fractionation arrangements should be reviewed

by the Australian Health Ministers' Conference in consultation with relevant parties and, where appropriate, upgraded in line with world's best practice.

4. The ARCBS needs to enhance innovation in its marketing efforts and customer service strategies in order to recruit donors from a broader cross section of the Australian community and to retain existing donors. In particular, there is a need for new strategies for encouraging more young Australians and members of ethnic communities to donate blood. The ARCBS will need additional funding support from governments to develop and implement such strategies. In the future, consideration may need to be given as to whether travel costs incurred by blood donors and plasma donors should be reimbursed or permitted to be treated as an allowable taxation offset; taxation offset for costs incurred as a direct consequence of blood or plasma donation would be a powerful statement of the importance attached by Government to the voluntary donation of blood.

5. The present annual planning and budgeting framework for plasma supply should be reviewed, with a view to moving to a four- to five-year business planning cycle. The current annual planning cycle is not consistent with best practice in strategic planning and can limit capacity for ensuring operational efficiency.

6. Uniform provisions concerning the age at which a person is eligible to donate blood should be introduced by all state and territory governments. A uniform approach along the lines of the system operating in South Australia would be in the best interests of collections by the ARCBS.

7. There should be greater consistency between states and territories in the application of revised national guidelines for IVIg usage.

8. The Therapeutic Goods Administration regulatory base should be revised to provide explicitly for the conduct of unannounced audits of overseas manufacturers. The new arrangements should be supported and confirmed through either Mutual Recognition Agreements or provisions in contracts with manufacturers. Consideration should be given to negotiating amendment of the Australia–EC/EFTA MRAs, to enable joint inspections of manufacturers of high risk medicines (including plasma products) by the TGA and designated EC/EFTA GMP inspectorates, where appropriate. Consideration should be given to amending the Therapeutic Goods Regulations to ensure that fees may be imposed on Australian product sponsors to cover the costs of GMP auditing of overseas manufacturing sites.

9. The Australian Health Ministers' Conference should continue to monitor and assess industry developments, with the aim of ensuring that the range of Australian plasma derived products remains appropriate to clinical requirements.

10. Australia should maintain its reservation regarding the procurement of blood fractionation services under the Australia–United States Free Trade Agreement. The reservation exempts the procurement of plasma fractionation services from the government procurement provisions in Chapter 15 of the Agreement. The CSL Act should also be maintained.