Dr Hilary Bambrick
Research Fellow
National Centre for Epidemiology and Population Health
The Australian National University
Canberra ACT 0200 Australia

T: +61 2 6125 8595/ 0438 120605
F: +61 2 6125 0740
E: hilary.bambrick@anu.edu.au
www.nceph.anu.edu.au

The Secretary
Review of Australia's Plasma Fractionation Arrangements
Department of Health and Ageing
plasmafractionationreview@health.gov.au

13 April 2006

Dear Secretary,

Attached is our submission to the Plasma Fractionation Review Committee. Specifically our submission addresses Terms of Reference 2 (appropriate requirements to ensure safety), 3 (issues arising from increased competition) and 4 (impact of competition on quality, efficacy, security of supply).

As doctors, epidemiologists, economists, lawyers, public health experts and blood donors, we list our concerns over the impact on the supply and safety of Australia's blood products of establishing a tender process for plasma fractionation. In particular we note that the emphasis on economic efficiencies will come at the expense of public health as manufacturing costs are reduced. We consider hazardous the loss of national autonomy in ensuring product safety through reduced capacity to regulate and monitor manufacturing processes and products, and the risk of delay and interrupted supply, particularly in the event of a large-scale emergency. Furthermore, a new, economically competitive tender process for one facet of blood product supply (fractionation) would in time extend into other areas including blood collection, eroding voluntary, non-remunerated donation which remains its strongest safeguard.

Of additional concern is that any tender would be open to dispute for even a non-technical breach under the non-violation nullification of benefits article included in the AUSFTA, broadening the scope of potential trade dispute from an actual breach to include any alleged breach of the spirit of the agreement.

The public health consequences of opening Australia's plasma fractionation services to overseas contract will extend beyond our national borders, affecting supply and quality in countries to which Australia currently provides fractionation services. Furthermore, there are substantial international health and ethical implications as the proposed changes would expand Australia's role in the growing international blood trade, and there would be further pressure on Australia to accept unsafe products from other countries.

Australia's blood and plasma products are currently among the safest in the world, but this position will probably be diminished with the introduction of overseas competition. Short term economic efficiencies should never be accorded greater importance than public health.

Sincerely,

Dr Hilary Bambrick
Dr Dorothy Broom
Dr Thomas Faunce
Professor Terry Hull
Mr Omar Ibrahim
Ms Kellie Johnston
Dr Chris Kelman
Ms Tanya Mark
Mr Colin McCulloch
Dr Rosalie Woodruff

Submission to the

Review of Australia's Plasma Fractionation Arrangements

April 2006

Dr Hilary Bambrick
National Centre for Epidemiology and Population Health, ANU

Dr Dorothy Broom
National Centre for Epidemiology and Population Health, ANU

Dr Thomas Faunce
ANU Medical School and ANU Law School

Professor Terry Hull
Research School of Social Sciences, ANU

Mr Omar Ibrahim
National Centre for Epidemiology and Population Health, ANU

Ms Kellie Johnston
ANU Law School

Dr Chris Kelman
ANU Medical School and National Centre for Epidemiology and Population Health, ANU

Ms Tanya Mark
National Centre for Epidemiology and Population Health, ANU

Mr Colin McCulloch
National Centre for Epidemiology and Population Health, ANU

Dr Rosalie Woodruff
National Centre for Epidemiology and Population Health, ANU

1. Australian blood safety should not be taken for granted

Australia is currently self-sufficient in its blood supply and in the majority of blood and plasma derived products. It imports only a limited number of therapeutic products, most of which use recombinant technology.

The safety of the Australian blood supply should not be taken for granted. It is essential to minimise the risk in receiving blood and blood products, not only selecting the source of blood and plasma, but by ensuring that manufacturing protocols are of the highest possible standard and are rigorously implemented.

2. Competitive tender would increase pressure to cut manufacturing costs

Striving for economic efficiencies to produce the most competitive tender can jeopardise public health. Economies of scale cannot be translated into the blood sector.

In manufactured blood products, the risk of infection from contamination is not limited to the direct relationship between donor and recipient. The larger the batch, the lower the manufacturing costs, as there is less cleaning and re-setting of equipment, but large batches increase the risk of contamination. For example, if plasma from 1000 different donors is pooled, the risk that the manufactured product is contaminated is increased 1000-fold. As the risk of contamination rises with larger batches, so too does the number of affected recipients. The capacity for timely recall of affected products will be diminished, and donor tracing becomes more difficult and takes longer.

Processing the smallest feasible batch is safer; if a problem occurs in manufacture or the batch is found to be contaminated, a minimum number of people are affected and the least donated plasma is wasted. Smaller batches are protective as each separate batch provides an alternative source in the event of possible contamination.

If a large United States company uses its economies of scale and legal expertise with complex procurement documents to undercut local providers in a tendering process, plasma donated in Australia could be shipped overseas for fractionation, and then returned. In such circumstances, rigorous cleaning of equipment between batch runs could not be well monitored. Variant Creutzfeldt-Jakob Disease (CJD), for example, resists detergents and autoclaving.[1] A successful overseas tenderer could potentially take over the CSL plant, but resultant ‘efficiencies’ may incrementally introduce standards and practices less effective than those presently in place.

Increasing competition in plasma fractionation may drive down manufacturing costs, but at what price to public health?

3. Off-shore manufacture would diminish national sovereignty and Australia’s ability to regulate and monitor the sector effectively

Subjecting the processing of Australia’s blood products to international trade rules reduces the capacity of Australian governments to make or uphold regulations to safeguard supply. Unless such regulations are specifically exempted, they may be treated as unnecessarily restrictive of trade. This is especially the case for regulations made to protect against *possible* risks rather than against existing risks that can be quantified. Extrapolation from what is understood about known risks to possible future risks is considered by Australia’s trading partners to be unnecessarily restrictive. Thus regulations in place to insure against unquantifiable risks or an as yet unknown disease are open to dispute. Australia is regularly criticised by trading partners for its cautious approach to quarantine in other sectors, such as agriculture, with opponents arguing that its risk assessments are “not based on science”, without recognising that real science is dynamic and incomplete.

Cautious trade practice is what protected Australia against bovine spongiform encephalopathy (BSE) when the specific risks of certain agricultural practices were still unknown. Such caution is

similarly warranted in blood products. Medical science is merely a work in progress; not all known diseases can be tested for, and more will emerge. Protection of public health is justified and is not the same as protectionism.

4. A competitive tender would be subject to the non-violation nullification of benefits article in AUSFTA

Uncertainty in what constitutes a trade barrier is made even more complex under the AUSFTA side letters, in which Australia is committed to recommend a tender linked to a non-violation nullification of benefits (NVNB) article in chapter 21.2(c). An NVNB article means that even in the absence of a *technical* breach, it may be claimed that the *spirit* of the agreement has been contravened, broadening the scope for trade disputes. The World Trade Organization (WTO) has held that such claims require detailed justification and, despite United States objections, has recently extended a moratorium on their use under the Trade Related Intellectual Property Rights (TRIPS) agreement,[2] and has stated that they should be 'approached with caution and should remain an exceptional remedy'.[3] However, the WTO explicitly left open the question of whether a party could have 'reasonable expectations' for NVNB purposes in relation to 'continued market access for products which are shown to pose a serious risk to human life or health.'[4] The NVNB article means that procurement contracts under AUSFTA are much more open to dispute than sustained by the WTO in other agreements.

5. Off-shore manufacture could lead to delays and interruptions to supply

Off-shore manufacture could disrupt blood supply, particularly in the event of a large-scale emergency such as a terrorist attack. Turn-around time to end-product would be increased, and in the case of a disaster requiring large amounts of fresh product quickly, there would be delay in returning any plasma awaiting processing, even if this were at all feasible (which it might not be).

Additional layers of complexity are added to processing and shipping as these would be directly subject to overseas legislation, as well as economic and political forces and disruption (affecting, for example, transport or industrial relations). With onshore manufacture such disruptions are more open to being handled 'in-house' in a timely fashion. Also, the risk of a substantial loss of blood products during the process of transportation (either via accident or a deliberate act of terrorism) increases with distance travelled.

6. Opening one area of the blood sector to competition opens the door for other areas to become subject to competition

The current battery of safety tests performed on blood collected in Australia is not perfect in either its coverage or accuracy, therefore donors are restricted to people who are healthy and considered to be at low risk of blood-transmissible disease. For example, the Australian Red Cross does not accept donations from people who have been in prison within the previous 12 months, or those who have had a recent tattoo or piercing. Blood cannot be screened for as yet unidentified or newly emergent diseases, as transmission of HIV and Hepatitis C to blood product recipients in the 1980s in Australia (and elsewhere) attests. There is still no blood test to detect variant CJD. It is therefore crucial that blood and plasma be sourced from lowest risk donors, and this means non-remunerated, volunteer donors, who are known to be the safest source.[5, 6]

The AUSFTA exchange of side letters states that Australia will no longer require that blood products imported from the United States demonstrate significant clinical advantage. This opens up the possibility that Australia will import blood and plasma products even where this is not necessary on clinical grounds. Much of the blood collected in the United States is from paid 'donations' which is demonstrably less safe than blood collected from non-remunerated donors. United States companies also buy blood from the poor in developing countries – people who tend to be in worse health, poorly nourished and desperate for income. Ethics and health detriments to these 'donors' aside, blood sourced from such populations puts recipients at considerable risk because (as

discussed above) tests for infection conducted on samples are imperfect, there are no tests for some known serious diseases, and newly emergent diseases may pass undetected. Blood bought from the poor in developing countries and processed in the United States is effectively laundered (see section 8) – its exact origins are unknown, and in the case of evident contamination, specific donors can never be traced.

As imports from the United States are no longer required to demonstrate clinical advantage over a locally produced product, we argue that they must at least be clinically *equivalent*; any imported products must also meet Australian standards and expectations of safety. They must be derived from non-remunerated, volunteer donors who have undergone the same level of donor screening and blood testing as is undertaken in Australia.

Other countries sell blood and plasma to the United States for processing and re-export (see Section 8). In the long run, these countries may attempt to sell to Australia directly. Lowering the regulatory protection for imports from the United States means Australia will have to accept products merely processed in the United States but sourced elsewhere, and it establishes a precedent enabling products to be imported directly from other countries, for example India and China. Such countries will be more easily able to challenge Australia on import restrictions.

There is nothing in AUSFTA to prevent future tendering for the *collection* of blood and plasma by for-profit companies as well its processing, potentially igniting competition for donors, loss of reliance on volunteer donations and consequently reduced safety of the blood supply. In the United States, for example, for-profit collection agencies compete for donors, offering money, prizes and financial incentives ('finder's fee') for introducing new donors to a collection company.[7] Plasma donors receive about US$25 per donation or up to US$200 per month, depending how often they donate, their blood type and specific antibodies.[8] Buying blood is not in the national interest. Safety of supply is compromised when blood 'donation' becomes a financial transaction rather than an act of altruism. Reviews have consistently found that such paid blood donors have higher rates of infectious disease, are more likely to donate in symptomless window periods,[9] and are at higher risk of emerging infectious diseases.[10] In short, blood sourced from paid 'donors' is less safe than blood from genuine donors.[5]

There is incentive, especially among the poor, to lie about one's medical and social history and to sell blood more often than is safe for the donor. This is bad for the donor and bad for the recipients who are more likely to receive contaminated and substandard blood products. Such factors have led to major concerns about the safety of blood products in the United States.[11]

There is also no evidence that offering payment to 'donors' increases their number. A recent survey in the UK found that almost the same number of current (non-remunerated) donors would be less likely to donate if they were paid as the number of non-donors who said they would consider becoming 'donors' if there was a payment.[6]

7. Changing Australia's fractionation arrangements will affect products in other countries

CSL Ltd in Australia is also the national provider of fractionation services to New Zealand, Malaysia, Hong Kong and Singapore.[12] New Zealand, for example, sends 38500kg of plasma for fractionation annually to Australia for processing, which is then returned to New Zealand as manufactured product.[13]

If CSL is no longer processing Australia's plasma, it may no longer be able to provide a cost-effective service to these other countries, forcing them to send their plasma further afield. Also, due to Australia's agreement with New Zealand to establish a Trans-Tasman joint regulatory agency on therapeutic goods, New Zealand may also be required to open its own processing arrangements to tender, or will be forced to piggy-back with new Australian arrangements. Furthermore, the advent

of the joint agency has the capacity to significantly influence the framework and standards under which the New Zealand Blood Service (NZBS) operates. In particular NZBS is concerned that regulations will be imposed rather than developed through an interactive process with the new regulator.[13]

The advent of the joint agency could potentially lead to Australia and New Zealand being treated as a single, larger source of blood and plasma and a single market in buying back blood products, with no differentiation between the two. If the high standards of each country are maintained, this may not be a safety issue, although it could become a political one if one country's donations were perceived to be shoring up the blood supply of the other.

Without the contract to provide Australia's plasma fractionation services, CSL Ltd may no longer be able to provide these services to other countries. Changes to Australia's fractionation arrangements will thus subject New Zealand, Malaysia, Hong Kong and Singapore to considerable uncertainty in their respective nations' supply of blood products.

8. Introducing overseas competition to provide fractionation services will increase Australia's participation in the global blood trade

Companies in the United States buy blood from the poor in developing countries. Blood is a scarce global commodity; paid donors in developing countries are a now a major source of the world's plasma [14], as the poor sell their plasma to international pharmaceutical companies for fractionation (for a fraction of the price paid to United States donors). Paid donors in developing countries are also at risk of infection at the time of donation, through re-use of equipment and injection of human blood; for example, widespread infection during plasmapheresis is known to have occurred in Mexico, India and in China [14]. Plasma products sourced from paid donors in developing countries have caused outbreaks of infection in recipients in developed countries, such as Hepatitis C among people with haemophilia in Ireland, Italy, France and Spain. Ireland is currently preparing to sue the United States company, Baxter, over this contamination.[15]

The safety of Australia's blood supply makes its fresh plasma and manufactured products premium products. The value of safe blood from Australia (and New Zealand) may be such that a special market is created. Overseas manufacture provides considerable opportunity for the siphoning off of premium quality products for sale to other countries or rich individuals. There can be no guarantees that the returned product is manufactured solely from Australian-sourced plasma, not 'diluted' with cheaper, higher risk plasma.

9. Risking the safety of Australia's blood supply is an equity issue

Failing to ensure that national blood supply is as safe as possible disproportionately affects one section of the population more than others. People with serious blood disorders such as haemophilia have a lifelong reliance on blood and plasma products and are the first to be affected by any contamination. This has been demonstrated repeatedly in Australia and elsewhere with newly emergent disease such as HIV and Hepatitis C. It is therefore imperative that the source of supply remains as safe as possible, and that strict regulations surrounding manufacture are impervious.

10. Increasing the commercialisation of blood damages its status as a gift

Australia's self-sufficiency in blood supply relies on goodwill; many donors give blood regularly. Donation takes time and disrupts work and routine. Some donors view their ability to donate as a national duty, some take great pleasure in knowing that they are able to save lives by donating [16]. Knowing that one's donated blood and plasma is being sold to an overseas company to be bought back may alter the way regular donors feel about 'giving' their blood. Some regular donors canvassed informally by the authors about the potential changes expressed dismay at the idea of their blood being so overtly commodified. As donors become more distanced from their gift; it may no longer be seen so clearly as something that directly helps their fellow Australians. Eventually

there may be a decline in donations, a loss in Australia's self-sufficiency in supply, and a move to reliance on overseas-sourced products.

11. Conclusions

On public health grounds we recommend against opening a tender process for plasma fractionation services. Tendering for services from the United States could have major and enduring consequences for the Australian healthcare system, Australia's self-sufficiency in blood supply from low-risk donations, its ability to regulate appropriately and monitor effectively, and its capacity to respond to natural and other disasters.

If an open tender process were recommended by the review, it would be linked to the NVNB article in the AUSFTA. This considerably broadens the scope for potential trade disputes beyond even that considered reasonable by the WTO. In the event of a trade dispute, even one based on claims of a non-technical breach, history has demonstrated that dispute settlement will favour 'free trade' over the protection of public health.

To ensure that blood safety in Australia remains at the highest level possible, it is necessary that:

- Regulations (such as those governing batch size) are not eroded;
- Australian regulatory control is not diminished;
- Cautious regulations cannot be considered restrictive trade practices; they must be respected as necessary to protect population health and excluded from future negotiation;
- Strict adherence to regulations and close monitoring continues;
- All blood and plasma used in Australia continues to be sourced from low risk, non-remunerated volunteers from Australia; and
- Testing for infection remains rigorous.

To ensure that the supply of safe blood and plasma products is not interrupted it is necessary that:

- Plasma processing remains on-shore.

Competing interests

An author of this submission, Hilary Bambrick, is related to the Chair of the Review Committee, Philip Flood. Mr Flood has had no input into this submission.

References

1. Taylor, D.M., Inactivation of prions by physical and chemical means. *J Hosp Infect*, 1999. **43 Suppl**: p. S69-76.
2. *Scope and Modalities of Non-Violation Complaints Under the TRIPS Agreement.* 2000, World Trade Organization Document IP/C/W/194 (Communication from the United States).
3. *Japan - Measures Affecting Consumer Photographic Film and Paper*. 1998, World Trade Organization Document WT/DS44/R [10.37] (Report of the Panel).
4. *European Communities - Measures Affecting Asbestos and Asbestos-Containing Products*. 2000, World Trade Organization Document WT/DS135 [190] (Report of the Panel).
5. Volkow, P., Y. Lopez-Vidal, R.I. Amieba, and M. Hernandez, Paid plasma donation and risk of blood-borne diseases in blood-product recipients. *Lancet*, 2001. **358**(9297): p. 2001-2.
6. Jones, R.P., V. Prasad, J. Kuruvatti, N. Tahir, *et al.*, Remuneration for blood donation and attitudes towards blood donation and receipt in Leeds. *Transfus Med*, 2003. **13**(3): p. 131-40.
7. International BioResources, *Earn Money and Save Lives*. 2006.http://www.internationalbioresources.com/Donor.cfm. 10 February 2006.
8. National Plasma Centers, *National Plasma Centers*. 2006.http://www.nationalplasmacenters.com/. 28 February 2006.
9. van der Poel, C.L., E. Seifried, and W.P. Schaasberg, Paying for blood donations: Still a risk? *Vox Sang*, 2002. **83**(4): p. 285-293.
10. Schreiber, G.B., M.P. Busch, S.H. Kleinman, and J.J. Korelitz, The risk of transfusion-transmitted viral infections. *N Engl J Med*, 1996. **334**(26): p. 1685-1690.
11. AuBuchon, J.P., J.D. Birkmeyer, and M.P. Busch, Safety of the blood supply in the US: opportunities and controversies. *Ann Int Med*, 1997. **127**(10): p. 904-909.
12. Commonwealth of Australia, *National Blood Authority Annual Report 2004-05*. 2005: Canberra.
13. New Zealand Blood Service, *Statement of Intent 1 July 2005 - 30 June 2006*. 2005.
14. Volkow, P. and C. Del Rio, Paid donation and plasma trade: unrecognized forces that drive the AIDS epidemic in developing countries. *Int J STD AIDS*, 2005. **16**(1): p. 5-8.
15. Finnegan, G., *Hep C scandal company gets E6m bird flu contract*. 2006.http://www.irishmedicalnews.ie/articles.asp?Category=news&ArticleID=15941. 13 April 2006.
16. Titmuss, R.M., *The Gift Relationship: from Human Blood to Social Policy*. 1970, London: Allen & Unwin.