

> Establishment of a Standing Offer for overseas-sourced Intravenous Immunoglobulin

In 2004, the National Blood Authority (NBA) was directed by the Jurisdictional Blood Committee (JBC), on behalf of all Australian Governments, to establish a 'Standing Offer' for a contingent supply of intravenous immunoglobulin (IVIg) from overseas.

Following a competitive, open tender process, the NBA established the 'Standing Offer for Supply of Overseas-Sourced IVIg' (IVIg Standing Offer) on 17 December 2004. Its purpose is a performance-based arrangement whereby Australian Governments can access overseas-sourced IVIg in order to meet any future shortfalls in the supply of domestic IVIg, if and when required. The NBA expects the Standing Offer will provide access to an alternative, secure source of IVIg at a competitive price.

The Offer currently involves two products and their suppliers:

- (i) Octagam distributed by Octapharma; and
- (ii) Sandoglobulin distributed by CSL Bioplasma.

It is expected the Standing Offer will include more suppliers as their products become registered on the Australian Register for Therapeutic Goods (ARTG) after being evaluated for product safety and efficacy by the Therapeutics Goods Administration (TGA) for supply in Australia. The Standing Offer does not guarantee the purchase or volume of any IVIg product(s) from a supplier on the Standing Offer.

There are two components to the Standing Offer:

1. A National Blood Supply (NBS) component: This component can only be

utilised with the approval of the JBC, to meet any shortfall in the domestic supply of IVIg. Any purchase from this component of the Standing Offer will be paid for by the NBA, under the Commonwealth/State and Territory Government cost sharing arrangements for the blood and blood products sector. This includes the potential for purchase of product for the National Reserve of plasma-derived products.

To date, both Sandoglobulin and Octagam have been purchased for the National Reserve. To avoid outdating, there will be a requirement to roll-out both products from the National Reserve to jurisdictions. The roll-out of Sandoglobulin has already commenced in four jurisdictions (QLD, NSW, VIC and SA). This process is being coordinated by the IVIg User Groups in the relevant jurisdictions in consultation with ARCBS, the NBA and the supplier. The roll-out of Octagam is anticipated to take place later this calendar year. A full communication plan for the roll-out of Octagam is currently being developed by the NBA in consultation with the ARCBS, TGA, the supplier and other key stakeholders.

2. A Jurisdictional Direct Order component: Approved State or Territory Recipients may place an order directly with the supplier for the IVIg product/s. Any purchase from this component of the Standing Offer will be paid for in full by the Approved Recipient (i.e. the requesting hospital).

More information on the Standing Offer is available on the NBA website at: www.nba.gov.au

> Our website has moved

The new Transfusion Medicine Services web address is: www.transfusion.com.au. This move from the old address of www.donateblood.com.au/clinical is intended to make our site easier to locate, for you and all interested healthcare professionals.

Initially, visitors using the old web address will be redirected to the new location.

If you encounter difficulties finding any information on our site, please e-mail clinicalinfo@arcbs.redcross.org.au

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> A national haemovigilance system in Australia?

Haemovigilance has earned a great deal of coverage in the medical literature, and rightly so. According to the European Blood Directive 2002/98/EC, haemovigilance is "a set of organised surveillance procedures relating to serious, adverse or unexpected events or reactions in donors or recipients, and the epidemiological follow-up of donors" (Faber, 2004 Oct). This definition embraces much of what we do in blood banking and transfusion medicine, no matter how you spell it, or whether you use the word at all (Heier 2000; Menitove, 1998).

Australia currently does not have a centralised national reporting system for adverse events to transfusion. Evaluation of such events occurs mainly at hospitals through their Transfusion Committees, with input from ARCBS as required.

It has been proposed that Australia adopt a haemovigilance system. In order to establish such a system in 2002, the Australian Commonwealth Department of Health and Ageing awarded a tender to consider issues related to a national blood transfusion monitoring scheme and to develop a suitable model.

In October 2004, a draft report prepared for the Australian Council for Safety and Quality in Health Care by Associate Professor Neil Boyce and Dr Chris Brook was broadly circulated for comment and consultation. The report reviews the current issues influencing appropriate transfusion governance within Australia and supports the implementation of a haemovigilance system.

The report states: 'It is important that this measurement program consciously focuses on monitoring aspects of transfusion performance where there is known to be great potential for delivering improved patient safety. Thus haemovigilance measures in an Australian transfusion context need to include both traditional product safety and clinical practices such as transfusion appropriateness. There must be a commitment to infrastructure that would enable transfusion practice improvement to occur if we are to embrace any national system of haemovigilance, as there is little point in measuring transfusion performance if there is no capacity to respond to any identified performance concerns'.

Likely, a mandate will emerge in Australia to create a national system of haemovigilance, which may be driven by changes in regulatory requirements. To view this article in full, visit our web site at: www.transfusion.com.au/files/news/haem.pdf

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> Change in ARCBS donor haemoglobin selection guidelines

ARCBS has recently introduced changes to the acceptable levels of haemoglobin for whole blood donation. From 1 January 2005, the Haemoglobin (Hb) threshold for whole blood donors increased by 2 g/L. The new levels increased the male whole blood donor threshold for haemoglobin to 130 g/L and the female threshold to 120g/L. This is the second and final phase of the program which began in January 2004.

The adjustment is being made to comply with regulatory requirements and to ensure that the small temporary drop in Hb experienced after blood donation does not allow donors to fall below normal levels. Haemoglobin acceptance levels for apheresis donors will remain the same. These levels do not apply to patients presenting for autologous collections.

ARCBS has undertaken a significant donor education program in nutritional health to prevent donor deferral and assist deferred donors in returning. There are also programs to increase both the recruitment and return rates of donors and to encourage suitable donors to increase their donation frequency.

ARCBS has also introduced ferritin testing, an indicator of iron stores, for all donors who do not meet required Hb levels. As a result of expanded national ferritin testing capabilities, ARCBS Medical Officers will be referring more patients to their GPs to investigate their iron status.

Should you have any queries in relation to the changes in haemoglobin levels and the potential for impact on the blood supply, please do not hesitate to contact a member of the Transfusion Medicine Team in your state or territory:

www.transfusion.com.au/Miscellaneous/ContactUs.asp

> Australia sends tetanus immunoglobulin to Aceh

As part of the relief efforts in tsunami-affected Indonesia, Australia has provided tetanus immunoglobulin (TIG) to Aceh province. This includes supplies of both the intravenous form for high-dose passive immunisation (as part of the treatment of clinical tetanus) and the intramuscular form for low-dose passive immunisation (as part of the management of patients with tetanus-prone wounds).

Whilst the amounts supplied are substantial, in keeping with the scale of the disaster and its aftermath in terms of disease and suffering, Australia has retained sufficient stocks to meet anticipated local needs of both low dose for intramuscular use and high dose for intravenous use.

> NAT testing enhances safety of Australia's blood supply

In June 2000, ARCBS added another layer of safety for blood products with the roll out of Nucleic-acid Amplification Technology (NAT) to test for the Hepatitis C and HIV-1 viruses. NAT has been used since then to complement the serological tests already in use. At the time of implementation, only two other countries, the USA and Germany, used NAT to screen donors for both HCV and HIV; ten others used NAT for HCV alone.¹

NAT amplifies a small segment of the target genetic material (DNA or RNA) over one million fold, making it extremely sensitive. By implementing NAT testing, the window period during which an infection may go undetected is significantly reduced from approximately 66 to seven days for HCV, and from 22 to nine days for HIV, compared to antibody testing alone.²

NAT does not replace antibody testing, as each test may detect carriers in different phases of viral infection. For Hepatitis C, about twenty five per cent of donors exposed to HCV have antibody only and may potentially be infectious, while some carriers may have fluctuating levels of viremia.³

NAT is however a complex system and, as the technology is not yet suitable for large throughput screening, blood services screen donations in pool sizes ranging from on average 16 to 961. ARCBS screens 80 per cent of donations in pool sizes of 24 and 20 per cent in single donation format.

In Australia the NAT yield (i.e. the rate of NAT positive but antibody negative donations) has approximated that predicted by ARCBS modelling.⁴ 11 window period donors have been intercepted by NAT screening of 4.7 million donations: nine in the HCV window and two in the HIV window.

Follow up on nine donors has so far confirmed all were in the early antibody-negative, pre-seroconversion window phase. Therefore, NAT prevented more than 26 potentially infectious fresh blood components, prepared from these 11 donations, from entering the blood supply, being transfused or from being sent for further processing.

In the latter case, some plasma components, although subject to very effective viral inactivation procedures, if pooled for further fractionation, may have multiplied the potential impact on products. Regardless of the risk, this would eventually necessitate patient and product recall with potential impact on supply.

In the USA, where over 40 million donations have now been screened, NAT is detecting HCV at about one in 270 000 donations and HIV at about one in 3.1 million.⁵ In the USA, with greater absolute yield numbers, the majority are in the window phase, however about five per cent carry the virus but never produce antibody - referred to as immunosilent. Similar cases may be expected in Australia as the number of donors screened increases.

An additional benefit of implementing NAT was demonstrated in the USA in 2003. West Nile Virus (WNV) NAT testing was rapidly implemented in response to the WNV epidemic that spread across North America. No human WNV cases have been reported in Australia.

Nevertheless software and hardware upgrades to the ARCBS NAT system planned for the first quarter of this year will permit the addition of this screening test if ever needed, and decrease the donation pool size from 24 to 16.

In summary, NAT is detecting early window period donors at the rate predicted by incidence rate modelling, thus enhancing the safety of the Australian blood supply. Technological advances in automated NAT platforms, permitting high throughput, single donation testing as well as a larger range of pathogen targets, should eventually replace the existing first generation NAT screening systems.

This article can be reviewed in full with references at: www.transfusion.com.au/files/news/nattest.pdf

> Pharmacovigilance: drug safety and plasma products

Pharmacovigilance (Drug Safety) is the science of collecting, evaluating, researching and monitoring information from health care providers and patients on the adverse effects of therapeutic products. The aim is to identify new information about hazards, and to prevent harm to patients. Health professionals are encouraged to report adverse drug reactions (ADRs) to companies to ensure product safety profiles are kept up-to-date.

No medicine is entirely without risk. Although many ADRs are identified during clinical trials, the only way to obtain a more accurate safety profile of a drug is when it has been administered over a long period of time to large numbers of patients. It's also important to get information from patients of different ethnic origins, disease states, and age groups - that is, how the drug is administered in the community. Drug Safety monitoring therefore ensures up-to-date information on the safety profile of drugs, including warnings for patient groups that are at increased risk of ADRs, and steps that can be taken to minimise the risk.

Regulatory authorities such as the TGA in Australia require pharmaceutical companies to report serious ADRs to them and to conduct ongoing drug safety surveillance of their product portfolio. Sometimes regular safety update reports summarising these activities are also required, not only for conventional chemical drug products, but also for highly processed biologicals such as plasma products and those produced by recombinant technology.

CSL Bioplasma has a dedicated Drug Safety team in its Melbourne head office for the management of adverse reactions to its plasma products. When they receive an ADR report, it is entered into a pharmacovigilance database specifically designed for ADR recording and analysis.

For every ADR received, the reporter is acknowledged in writing and an ADR form is sent for completion of case details. A batch review is conducted for any previous ADRs, to see if there is a pattern of similar reports. An increased frequency in reports, especially if serious or unexpected in nature, will trigger further investigation.

For CSL Bioplasma plasma products, ADR reports can be sent to the CSL Bioplasma Medical Affairs department via their Medical Information Hotline: 1800 067 140 or email: drugsafety.bioplasma@csl.com.au.

> Blood bag tender evaluation update

The second phase of the ARCBS blood bag evaluations successfully concluded in November 2004. Approximately 3000 donations were collected into four different blood bags. Blood components were evaluated by ARCBS to ensure specifications were met and subsequently issued to a selection of hospitals in Sydney, Brisbane, Townsville, Melbourne, Adelaide and Perth for feedback from clinical and laboratory staff.

In total, 831 administration and 20 laboratory surveys were returned from 18 participating hospitals. Surveys were intended to compare the performance of the trial bags against those in normal use. The laboratory survey looked at aspects of storage, handling, cross-matching and labelling, whereas the administration survey focused on port access, hanging devices, filters and ease of spiking the port.

The number of administration surveys entered by each state is included in the table on the right. The responses to both surveys were analysed and the overall picture showed the trial blood bags were considered satisfactory. When compared to normal blood bags in use, the predominant response was of 'no difference' or 'marginally better'. A minority of responders identified a number of issues and these are being carefully reviewed as part of ARCBS ongoing relationship with blood bag suppliers. ARCBS wishes to acknowledge and thank those hospital staff who provided feedback. As a result of the successful Phase 2 evaluations, a pilot program of various new blood bags is due to commence in Queensland in June 2005.

State	No. of Admin Surveys
WA	193
QLD	223
VIC	48
NSW	149
SA	218

> Risk of transfusion-transmitted infection

ARCBS estimates of residual risk of transfusion-transmitted infection are based on the median value of three published models¹. The values in the table below detail the estimated risk for the period July 2000 to June 2003.

The figures for HIV and HCV antibody testing only are included to allow for risk comparison in the rare event that products are released without Nucleic Acid Testing (NAT).

Virus and testing standard	Window period (days)	Point estimate of residual risk 'per unit'
HIV 1 and 2 antibody only	22	1 in 2,404,000
HIV antibody + NAT	9	1 in 7,299,000
HCV antibody only	66	1 in 330,000
HCV antibody + NAT	7	1 in 3,663,000
HBV	45	1 in 1,339,000
HTLV I & II	51	Considerably less than 1 in 1,000,000
vCJD		Possible. Not yet reported in Australia ²

- 1 Assessing the accuracy of three viral risk models in predicting the outcome of implementing HIV & HCV NAT donor screening in Australia and the implications for future HBV NAT. Seed C.R. et al., *Transfusion* 2002; 42:1365-72.
- 2 vCJD: To date no Australian has been identified with vCJD. In the UK there have been two reported cases of probable transfusion transmission of vCJD in 2003/04. In Australia, as a precaution, people who have spent a cumulative period of 6 months in the UK between 1/1/80 and 31/12/96 and/or had a transfusion in the UK between 1/1/80 and the present time are not accepted as blood donors.



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