

**Response to the
National Blood Authority**

**Supply of Defined Blood Products-
Future Arrangements
Discussion Paper**

by the

**Australian Haemophilia Centre
Directors' Organisation**

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Introduction

AHCDO is the peak medical body for haemophilia and related bleeding disorders in Australia and its membership consists of the medical directors of Haemophilia Treatment Centres (HTCs). AHCDO was incorporated in Victoria in 2000 however its membership had previously met for many years as the Medical Advisory Panel of Haemophilia Foundation Australia. AHCDO maintains the Australian Bleeding Disorder Registry (ABDR), a database established in part to track prevalence, treatment and outcomes of people with bleeding disorders. It is in this context that AHCDO makes this submission addressing the questions raised in the Discussion Paper.

Response to Discussion Paper

Does the current suite of coagulation products referred to in this Paper meet the treatment needs of patients with bleeding disorders?

The coagulation products referred to in the Discussion Paper are recombinant FVIIa, recombinant FVIII, recombinant FIX, anti-inhibitor Coagulant Complex, protein C, plasma derived FVII, plasma derived FXI, plasma derived FXIII and Rh(D) Immunoglobulin.

Although von Willebrands factor is contained in the plasma derived FVIII product Biostate, we note that there is no specific mention in the Discussion Paper of this as a separate product. Since Biostate is not yet registered for use in patients with VWD it may be necessary to include a VWD factor concentrate with indications for surgery and prophylaxis in VWD as a Defined Blood Product.

Plasma derived fibrinogen concentrate is available and useful for afibrinogenaemia and dysfibrinogenaemia and therefore warrants consideration for inclusion.

Are there products in use overseas that should be considered for supply under contract in Australia? If so, describe their application.

Apart from the fibrinogen concentrate mentioned above, and notwithstanding the difference between first, second and third generation recombinant products, AHCDO is not aware of any other products currently used overseas that should be considered for supply under contract in Australia. Nevertheless, AHCDO is aware that the development of new products is underway and there needs to be a process whereby any new products which offer significant enhancements can be introduced within the life of the contract.

If new products are introduced during the contract period, how will this impact on patients?

Since our prime role is to administer the safest and best products to patients with haemophilia and related bleeding disorders, AHCDO strongly supports the provision of new products to patients, in circumstances where a clinical indication is shown or where increased safety is likely. On these grounds, AHCDO would like to see provision in the new supply contract to enable appropriate new products to be introduced during the life of the contract.

The introduction of new products will enhance quality of treatment and at the same time may introduce some competition in specific areas – eg management of those with inhibitors.

Should the NBA provide for clinician/patient choice of rFVIII products under the new supply arrangements?

Choice of product for patient and clinician has been traditional in USA and has been introduced in other countries eg UK. The decision to have more than one rFVIII product available in Australia is complex and all the issues require careful consideration.

Although a single supplier may allow for greater competition with in the market place and hence provide the best possible dollar price this financial issue is outside AHCDOs field of expertise and AHCDO will therefore restrict comments to clinical and practical issues which are relevant to its members.

AHCDO considers the risk to a constant and secure supply of rFVIII from a single supplier is unacceptable despite presumed provisions within the contract aimed at mitigating this issue.

Having multiple products available has many advantages – pure choice within equivalent products, ability to select a product with an emerging improvement (which is not known at the time of the tender), minimisation of the risk to supply and the availability of alternative products if a patient has a reaction eg allergic to one specific product.

Disadvantages to the availability of multiple products, including managing products in an inventory both within HTCs and outside HTCs and the planning of usage within the tender, should be acknowledged and may vary considerably between jurisdictions and HTCs. Nevertheless AHCDO considers that the advantages of multiple suppliers outweigh the disadvantages and would recommend that two or more rFVIII products are available in Australia through the new Defined Blood Products Agreement.

Consideration should also be given to the equivalence of the available products. Although all products must be licensed within Australia and listed on the Australian Register of Therapeutic Goods there may be subtle differences, eg pertaining to safety, between the products which may make one product preferable to another.

How would the NBA manage supply at the clinical level if there is more than one rFVIII product available?

There are multiple ways to manage the inventory, for example either each state or HTC or split between adult and paediatric centres, however these methods would mean that true clinician and/or patient choice is lost.

How ever this complex issue is eventually managed it should be remembered that most clinicians will be reluctant to change patients between products due to case series which have demonstrated a risk of inhibitor development. The gradual introduction of additional rFVIII products would allow new patients (and some current patients) to use an alternative product for the long term. Wholesale product change at each tender should be avoided. Clear guidelines regarding supply limits of any alternative rFVIII product will limit its use in the HTCs. AHCDO notes that this model has worked successfully in Canada.

In some smaller HTCs managing multiple products may be harder than others and may require additional resources. These possible difficulties could be mitigated by the supply of a maximum of two products during the life of the tender.

This complex issue requires further consideration of the mechanics involved.

Should the NBA decide on a preferred supplier of rFVIII? If so, what criteria should the NBA apply to arrive at a preferred product?

AHCDO urges the NBA to contract at least two and possibly multiple suppliers for the provision of rFVIII. The continued provision of a single preferred product is not in the best interests of patients nor their clinicians. As there are on going developments in the manufacture of these products and in the experience of their clinical use, it is important that clinicians in Australia continue to gain experience in the use of a variety of products. Nevertheless, it may be possible for the NBA to identify more than one preferred product for which a preference can be expressed in terms of safety and efficacy as primary indicators, followed by secondary financial indicators, notwithstanding product registration with the TGA.

In terms of sufficiency of supply AHCDO believes that more than one supplier is the most prudent course of action to safeguard against product recall or plant failure. Past experiences have shown that product shortages, leading to possible postponement of treatment and compromise in optimal health care, can occur when a supplier is unable to meet demand.

Prior to the current Defined Blood Products Agreement being implemented most HTCs used one preferred product, usually based upon clinician or jurisdictional government choice; however we note that the Victorian paediatric HTC at the Royal Children's Hospital successfully used multiple products.

Much has been made of distribution networks. Currently the fresh blood products are distributed by ARCBS, fully government funded. Having multiple distributors working through both laboratory transfusion services and pharmacies only serves to increase complexity for clinician and patient and ultimately increases the cost of each product. Rationalisation of distribution networks needs to occur in the context of the tender process.

Is there a need for a gate-keeping role with respect to the Defined Blood Products? Who should have this role?

Due to the high cost, appropriate audit is necessary. The most expert clinicians in the use of these products are represented by AHCDO. Distributors such as ARCBS and private companies should not assume the role of "gate-keepers", having a lesser understanding of clinical imperatives. Establishment of "Factor Nurses" to assist in audit, recording and clinical assessments is an example of "grass-roots" gate keeping. This could be performed in collaboration with the Australian Bleeding Disorder Registry (ABDR).

The use of these defined blood products needs to be carefully monitored either after use or before use in a gate-keeping role. If HTCs do not have direct control over distribution there should be some mechanism set in place to facilitate communication and monitoring between the HTC and the distributor.

Is the ABDR a useful tool?

The ABDR has been in operation since the late 1990's when it was established by HFA. The registry includes data from all jurisdictions except New South Wales, however NSW Health has recently agreed to contribute data and mechanisms are currently being developed to facilitate this. Following the inclusion of NSW data, the ABDR will provide Australia-wide data relating to haemophilia and other bleeding disorders, allowing comprehensive analysis of trends in product usage and health outcomes and facilitating government policy development. The importance of the ABDR as a tool to identify trends within the haemophilia community should not be underestimated particularly given the high cost of treatment products. Nevertheless, it is equally vital that the ABDR is provided with sufficient funds to collect and analyse accurate and validated data.

The ABDR is also an important tool for research and data, after approval from AHCDO and the NBA, has been released to several educational and research institutions.

What is the experience of Haemophilia Treatment Centres in data collection and data entry for the ABDR?

Funding for data collection and data entry at HTC's was negotiated in to the ABDR funding agreement with the Department of Health & Ageing in 2003, however the funding did not become available until the end of 2004. Similarly, the ongoing funding agreement with the NBA provides data management funding at a level of 1EFT position shared between the HTC's in Victoria and Tasmania and 0.5EFT position shared between the HTC's in each of South Australia, Queensland and Western Australia. There is no funding available for HTC's in New South Wales.

Prior to the availability of this funding, when there was no dedicated data manager data entry was sometimes undertaken by busy clinical staff, however there were several large HTC's where there was no data collection for the ABDR.

In order to maintain accurate and complete data collection it is essential for sufficient funding to be available for data management. Although the current funding is a valued improvement and provides sufficient provision for basic data collection, it should be noted that more complex data collection is likely to require additional funding.

Some HTC's had previously been collecting data in a local data base and there appears to have been a small degree of reluctance to switch to the main ABDR, with a perceived view that the local database offered a wider range of relevant fields and ease of use. It is vital that a uniform core data base like the ABDR is employed through out Australia.

There is an increasing use of electronic means for collecting usage data and this may also include the collection of clinical data about site of bleed and treatment response. This data is valuable to AHCDO and the ABDR to help provide ongoing clinical oversight of the use of blood and recombinant products. The implementation of such an electronic data collection system would be beneficial to the Australian situation but funding to achieve this type of collection would be required.

It is pertinent that the ABDR was established on old technology and a small amount of capital upgrade would improve its efficiency. This should be considered as part of the current tender negotiations.

Are patients aware of the ABDR? If so what do patients think about the ABDR?

Clinicians have spoken with many of their patients regarding the ABDR and the important information that can be gleaned from the collection and analysis of the data with respect to improved health outcomes and supply and demand strategies. AHCDO has also written an article about the role of the ABDR for the HFA newsletter, *National Haemophilia*, published April/May 2005, which had a distributed of 1800. The ABDR, and health registries in general, will be the subject of discussion at a session at the forthcoming Haemophilia Foundation Australia conference, which many patients attend.

Patients should be confident that the ABDR complies with all appropriate privacy legislation and holds only de-identified information. Individual data is not released.

As the ABDR is a Commonwealth government endorsed Quality Assured Activity there is no need for clinicians to obtain formal written consent from patients. Nevertheless AHCDO believes the majority of patients are aware of the ABDR.

What other registries of blood coagulation products exist?

Registries exist in several countries including the UK, Canada and Italy, however AHCDO is not familiar with the exact type of data collected. AHCDO understands that registries exist in New Zealand, Ireland, South Africa, Russia and Thailand and that the Netherlands conducts a postal survey of patients every two years however it is not certain whether data relating to treatment products are collected in any of these countries.

Inter- and intra-continental registries exist for VWD and specific rare bleeding disorders which also address product usage issues.

The World Federation of Hemophilia compile an annual survey which collects limited product usage data from national haemophilia organizations where available.

Recently Novo Nordisk commenced a registry of use for NovoSeven in Australia.

Are there other off-label uses for any of the products referred to in this Paper?

At present Biostate is being used off label for the treatment of VWD. From clinical experience it is efficacious.

Recombinant VIIa is used off label for Factor VII deficiency and Glanzmanns thrombasthenia. AHCDO has published guidelines recommending its use for Factor VII deficiency and this product has been approved for both these indications in Europe.

RVIIa is also increasingly used in massive transfusion / microvascular bleeding and studies are underway to examine its use in trauma. Some indications eg post partum haemorrhage may never be studied in a randomised fashion. Consistent and clear guidelines are required for its use.

RVIIa is also used as reversal for Low Molecular Weight Heparin therapy, in particular longer acting preparations that may come onto the market or else be under investigation.

Is any off-label use an indicator of where demand or need may move to in the future?

The use of rVIIa in massive transfusion does indicate an increasing market. Although not yet incorporated into clinical practice, early clinical data of the use of rFVIIa in haemorrhagic stroke shows very promising results. Further data published during the life of this tender may indicate an increasing use of rFVIIa for this condition.

Biostate will probably continue to be used to treat VWD but this market penetration is to be expected. Newer agents with improved efficacy in selected functions may indicate new indications.

What, if any, would be the issues facing haemostasis laboratories if more than one rFVIII product were available under the new supply arrangements?

Previously it was necessary to use a different factor assay for Refacto compared to the other available rFVIII concentrates. It is understood that the newer Refacto can be monitored by a one stage factor assay as with others. This needs to be evaluated critically.

What policy and other issues are important to the haemophilia community with respect to the future supply arrangements?

The secure and reliable supply of appropriate treatment products is of significant importance to the haemophilia community.

The community also has questions regarding the international use of any “excess” Biostate manufactured from Australian plasma.