HAEMOPHILIA FOUNDATION AUSTRALIAN CAPITAL TERRITORY

PATRON
Major-General Peter Phillips, AO, MC

Review of Australia's Fractionation Arrangements
Department of Health and Ageing
GPO Box 9848
MDP 47
CANBERRA ACT 2601

Email: plasmafractionationreview@health.gov.au

Attn: Mr Phillip Flood (AO) – Review Chair

Review of Australia's Plasma Fractionation Arrangements - Submission

A. INTRODUCTION

Australia is envied by countries around the world for many reasons. For individuals who depend on blood products for their ongoing health and survival, Australia is seen as the lucky country because of its isolated blood supply and stringent safety regulations in the production of these important products.

Australians donate blood willingly and in return have access to safe, high quality blood and blood products free of charge. In the past, individuals with haemophilia have been the major consumer of plasma derived products in Australia, requiring plasma derived treatment factors to manage bleeding episodes. Whilst other conditions now drive the demand for plasma derived products, people with haemophilia are an important source of knowledge for this review as they have significant experience in dealing with complications that may arise from using treatment products originating from human sources such as plasma. The majority of the adult haemophilia community are currently living with the consequences of injecting plasma products infected with either HIV or Hepatitis C.

It is the responsibility of government, whatever the cost, to protect individuals using plasma products from known viruses, show vigilance in identifying other risks in all areas of blood collection and manufacture of plasma products and take immediate measures to eliminate or prevent harm to individuals.

B. DEMAND TRENDS FOR PLASMA PRODUCTS

Advances in haemophilia treatment tend to concentrate primarily on early treatment with recombinant products. Technologies associated with recombinant products focus on features such as sustained half-life and better delivery systems to compete with genetic treatments. In the future, complications for people diagnosed with haemophilia will focus on development of immune responses to treatment products and it is in this area where plasma products may play a role in the future of haemophilia treatment as an alternative treatment.

Physicians in Australia still tend to tolerise with plasma derived product although this may change in the future. There is an unanswered question regarding the transition to recombinant treatments post-tolerisation and whether this may trigger another irreversible immune response. As no assurances can be given by medical professionals on this issue, an individual in this situation must make a decision whether to trade-off known safety risks of staying with a plasma derived treatment product, against ineffective treatment caused by the return of an immune response to a new recombinant treatment product. The decision needs to be one that an informed individual makes in consultation with their physician.

Recombinant products will continue to be the optimal choice of treatment by physicians and people with haemophilia in Australia within the next 10 -15 years. Usage trends for recombinant products may steadily increase over that time as the remainder of individuals on plasma products transition to recombinant products and newly diagnosed patients start to use recombinant product from early stages of diagnosis. In the long term future, usage trends for recombinant products should stabilise to be based on the number of newly diagnosed patients.

Plasma derived products may be used as an alternative to recombinant products if an individual develops an immune response to recombinant treatment products. Plasma derived haemophilia treatment products manufactured in Australia currently rate among the safest in the world and are a viable option to recombinant in the case where there is no other alternative. The safety of Australian plasma derived products have significantly improved due to Australia's isolated blood supply, viral inactivation procedures and stringent regulation and checking at all levels of the blood collection and fractionation process.

The success of tolerisation within Australia has seen a steady increase in the number of tolerisation programs being performed by physicians over the last 5 years. This is very positive as successful tolerisation is a life-changing procedure for individuals who develop an immune response to treatment products. Current thinking on tolerisation is to tolerise as early as possible to prevent disability and pain. As tolerisation becomes an accepted treatment within Australian Haemophilia Treatment Centres, plasma products may be used to treat the older generation (yrs 30+) of individuals who develop immune responses to haemophilia treatment products. Any surplus plasma products could be used for tolerisation programs to greatly improve the lives of the forgotten older generation of people living with constant bleeding and pain. This may be a more cost effective treatment alternative for individuals who develop an immune response to treatment products than treatment on demand with Novo 7.

Plasma derived haemophilia treatment products will be required by a subset of the haemophilia community who need these products for the treatment of Von Willebrand’s Disorder, or as an alternative to recombinant product, or for tolerisation procedures. Those who have undergone tolerisation procedures may also wish to stay on current plasma derived treatment to eliminate the risk of developing another immune response to a foreign treatment product.

Uncertain times make it prudent to take into account the possibility of an event that may limit or cease the importation of recombinant product into Australia. If this scenario plays out, it will be critical for Australia to have the capacity to independantly produce plasma derived treatment product for its approx 1,800 citizens with haemophilia. It is in Australia’s interest to maintain the ability to internally fractionate and supply all plasma derived products in times of emergency. Significant national or world events may cause an increase in the demand for plasma products in an environment where Australia may not be able to source the services from international suppliers.

When identifying the effects a tendering arrangement may have on meeting demand for plasma derived products, it is important to consider the following:

Self Sufficiency

Awarding the contract to an off-shore supplier may leave citizens vulnerable in times where demand suddenly increases. Serious consideration needs to be given to keeping plasma fractionation capabilities within Australia to ensure provision in an unstable international environment. It is important to instigate fallback mechanisms to ensure that plasma products can be obtained through alternative channels in times where the supplier is unable to meet demand.

Supply

Having one supplier of critical plasma products may compromise the provision of adequate supplies of plasma derived products delivered in a timely maner. Government needs to asses and validate production levels and distribution mechanisms of potential service providers before any contract is entered into. It would be prudent for a cyclic reserve of plasma products to be maintained to cover the

production and distribution timeframes of any supplier or any shortfall of products that may result from unforseen incidents that may may adversely effect supply.

Accountability

Australia needs to ensure that any provider of such services performs effective fractionation where Australian blood is not wasted. Australian blood needs to be treated as a National Resource and as such its value needs to be assessed in terms of the cost of what goes out and what comes back. Australia needs to ensure that "the blood of the Nation" going off-shore is not syphoned off for other ventures that the fractionator may be involved with.

Responsibility of Government

Individuals donate blood for a number of reasons and have the perception of implied ownership. There may be a significant effect on the blood donation rate if Australian citizens see their blood going off-shore or if there is a perception of mismanagement of the blood supply. It is important for Australian regulatory bodies to try to forsee problems in the production of plasma products before they actually occur. Governments will compromise the ability to more closely track processes involved with the production of product if plasma fractionation services are externalised.

C. REGULATORY REQUIREMENTS

If plasma fractionation services are to be opened up to international markets, greater importance needs to be placed on safety, quality, auditing and regulation of plasma products coming into and going out of Australia. Australian citizens need to have the same level of confidence in the product as they do now.

The tendering process requires Government to have in place efficient processes, policy and regulations to measure and assess safety, quality and efficacy of plasma derived products. Given that Australia has stringent regulations at all levels of blood collection and manufacturing of plasma products that ensure world's best practice, can government confidently assure citizens using plasma derived products that the service provider selected in the tendering process will abide by the regulations set by the Government? Regular formal monitoring and assessment processes are required to maintain quality and safety. A concern is that fractionators may take short cuts in the fractionation process to deliver expected outcomes (eg. viral inactivation processes may be skipped to improve yield to win a contract).

Government requires a validation process to ensure products being supplied are manufactured from Australian blood only. What assurances can Government give to individuals using plasma products to ensure the plasma products supplied by the fractionator have not been contaminated by the various processes employed by the fractionator?

Any tendering arrangement would need to consider aspects related to immediate disclosure of information by both parties pertaining to elements affecting product safety, quality, supply and efficacy. Clear requirements regarding what constitutes a safety risk need to be formalised and clearly understood by both parties. Similarly, the contract needs to formally stipulate when parties must disclose information that may have implications to users of the plasma products as well as who must be informed. Efficient recall procedures and regulations need to be agreed on before any contract is entered into. Clear communication channels and professional relationships are required to effectively pre-empt potential problems with safety, supply, quality and efficacy.

Processes need to be formulated to successfully quantify the amount of Australian blood that leaves Australia as starting material and enters Australia in the form of plasma products.

A quality assurance process is required before products supplied by the fractionator are distributed to end-users to reassure them that the safety and efficacy requirements have been met by the fractionator. There is no guarantee that Australia will get back what it gives, or that the fractionator has abided by the regulations and conditions defined under the terms of the contract. Australian regulatory authorities require the establishment of processes that provide visibility into the fractionation and management processes of the fractionator.

There is an element of risk in the starting material of plasma products supplied by Australian Red Cross Blood Service (ARCBS). It will be critical to identify and formalise the risk of contamination in the starting material before it is sent to the fractionator. ARCBS needs to ensure the safety of the starting material and have clear agreements with the fractionator regarding when starting material can be safely used in production of product, given proper implementation of viral inactivation steps in the fractionation process.

Estimates of time to undertake end-to-end activities in the fractionation process are required to establish schedules for starting material and final product delivery. Fallback procedures are needed in the event these schedules cannot be met. There is a requirement to identify events and times where the fractionator may need to increase production due to an increase in demand for plasma derived products. The fractionator must understand the priorities of Australian supply during this time.

If an off-shore fractionator is selected, the government needs to consider issues outside the control of the fractionator in supplying starting material and delivery of the final product. The air freight industry and import/export legislation of foreign governments and how that may change in the future are factors that will impact supply in an off-shore arrangement. The government under which the fractionator operates may also impose restrictions on the import and export of biological products due to infectious disease control.

D. INCREASING COMPETITION

Australia's only local fractionator is CSL. CSL has strong ties to government despite its privatisation in the early 90's. There are negative and positive aspects in CSL's relationship with the Australian Government.

CSL is aware of Australian requirements and the workings of the Australian regulatory system. Government has some visibility and knowledge into how CSL works and its business practices. The Australian health community is familiar with plasma products that CSL produce. Government may compromise its relationship with CSL if it enters into fractionation agreements with off-shore suppliers which may encourage CSL itself to move off-shore to pursue larger markets. CSL moving off-shore will be a devastating blow to Australia both economically and in relation to self sufficiency. Government needs to instil some form of national responsibility within CSL’s management (if this does not take place already) to prevent this from happening. Retaining a contract with CSL as well as entering into a contract with a secondary off-shore supplier may make it viable for CSL to remain in Australia.

The negative aspect of CSL's relationship with government is that CSL has a monopoly on the Australian plasma market since its privatisation. This has resulted in an increased cost to Government as well as having a smaller range of products. It may be viable to retain a contract with CSL as well as entering into a contract with a secondary off-shore supplier. This may work if the market in Australia is large enough to support two suppliers of plasma derived products.

Opening health products up to competition instills the notion that "the bottom line" drives the provision of health services in Australia. This is a very big concern for recipients of plasma derived products as the majority of products offered at a reduced cost usually trade-off elements such as safety and quality. It is important that the safety of plasma products will not be compromised as a result of bidders offering cheaper products.

As mentioned above, increasing competition may compromise Australia's fractionation self-sufficiency by impacting management decisions at CSL to remain loyal to Australian interests. By establishing a number of contracts with different suppliers of plasma derived products and by ensuring that one of those contracts is with an Australian fractionator, Australia can limit its risk in terms of self-sufficiency, offer a broader range of treatment products to physicians and its citizens and open the market up to other service providers who can compete with CSL. A longer term option that may have far-reaching benefits for Australia would be to provide incentives to off-shore fractionators to establish fractionation facilities within Australia.

Security of supply refers to the continual and stable provision of safe and effective plasma derived products to Australian citizens who require them to maintain health and quality of life. Australia would significantly minimise its risk of reducing security of supply if it sourced plasma products soley from Australian fractionators or by maintaining a service provision contract with an Australian fractionator. Australia would be maximising its risk of ensuring security of supply by establishing a sole supplier agreement with an off-shore fractionator. The latter arrangement may significantly jeopardise continuity of care or timely availability of plasma derived treatments for Australian citizens requiring them.

For any contract established with a supplier of plasma derived treatment products, the following processes would minimise the risk of ensuring security of supply:

1. Determine accurate measures of the timing (best and worst case) of steps taken to produce each plasma derived product from collection of starting material to the dispensation of the final product.
2. Identify areas of delay that may occur at each of the steps in the production of each plasma derived process and determine contingencies for each delay.
3. Establish a cyclic reserve located in Australia to ensure supply of the product for the length of time of the delays, taking into account the contingencies.
4. Instigate open and honest communication channels with the fractionator to determine issues with supply as soon as possible and to instigate contingencies immediately.
5. Establish an effective agreed production schedule with the fractionator that meets the needs of physicians and individuals requiring products.
6. Instigate mechanisms to monitor, alert and communicate factors impacting the production schedule. The mechanism needs to establish communication channels with key stakeholders and have in place processes that trigger contingencies based on the alerts.

There are a number of costs that are associated with the importing and exporting of starting material and final product internationally. There may be additional costs associated with how the contract with a fractionation company is setup. There may be additional costs based on prioritisation of fractionation requests, or additional unforseen requirements imposed on fractionators after the contract has been made (eg. it may cost the government more if it asks the fractionator to ramp up production based on an over-supply of starting material or a medical emergency that requires a greater supply).

Listed below are some ways Australia can maintain safe, high quality, efficacious plasma products while increasing competition:

1. Give greater emphasis to safety, quality and efficacy over price. Costs associated with unsafe, low quality and ineffective treatments can cost government in other ways that will be significantly more expensive in the long term.
2. Determine effective and meaningful measures for safety, quality and efficacy within the regulations so that tenderers can be appropriately assessed.
3. Ensure that regulators have appropriate visibility into the collection and production process of the fractionator in order to monitor safety and quality.
4. Implement open, non-threatening and honest communication channels with the fractionator and collection agency so that safety issues can be highlighted immediately and action taken to minimise any impact of a safety breach.
5 Instigate effective and transparent record keeping through the government regulator. The regulator would be required to collect records from ARCBS, the fractionator and distribution points (eg. hospitals) which will enable the ability to track the impact to individuals relating to any safety breaches that occur.
6. Instigate and enforce unambiguous and effective recall regulations at all levels of the collection, production and distribution process to minimise any impact of safety breaches.

7. Perform supplementary Quality Assurance testing on sample batches of end product for viruses, specificity and purity.

Implications relating to the starting material relate mainly to the assurance that all known viruses have been eliminated prior to sending the material to the fractionator. There needs to be an optimal level of testing to ensure that the material does not contain any risk of known viruses within the starting material. It is important to have 100% level of confidence in the starting material. The level of confidence in the quality and safety of the starting material needs to be agreed on by ARCBS and the fractionator before it is used in the fractionation of plasma products.

Australian Red Cross would be best placed to manage the national reserve of plasma products. The reserve would have to be located within Australia, preferably at multiple sites around the country.

The roles of the various stakeholder organisations would need to change as follows:

1. The Therapeutic Goods Administration (TGA) charter could be expanded to manage the collection and storage of treatment records including the management of lookbacks when an incident occurs. TGA's role in managing safety and quality may become more difficult as it may not have the visability it once had within CSL. TGA would be responsible for validation, assessment and monitoring of fractionation processes to ensure safety, quality and supply.
2. The National Blood Authority (NBA) would need to co-ordinate compliance with regulations and requirements with respect to its affect on the contract. NBA would need to work closely with TGA and ARCBS to ensure regulations and production schedules are being met.

Off-shore companies will not be held accountable under Australian law for negligence in the production and supply process. Government need to ensure organisations or companies are held accountable in cases where negligence has resulted in adverse health to individuals using the plasma products. An advocate of Australians who use plasma products under any new arrangement needs to seek a legal opinion so that these individuals are represented and explained their rights under the possible new arrangements. Clear regulations need to be established relating to liability that properly protects individuals using these products.

Thank you for the opportunity to make a submission on these important matters.

Signed:

Fred Wensing

(President)
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On behalf of the committee of the
Haemophilia Foundation Australian Capital Territory Inc.
Address: GPO Box 936
Canberra City ACT 2601
Email: president@hfact.org.au