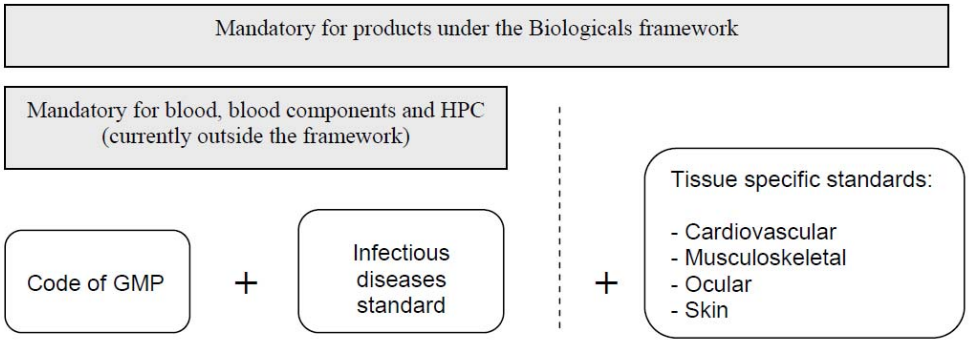
1. Background and scope

The TGA documents for consultation, the Code of Good Manufacturing Practice human blood and blood components, human tissues and human cellular therapies (Code of GMP) and the Therapeutic Goods Order (TG)) standards for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapies (infectious diseases standard) *will also apply* to products that are currently outside the scope of the Biologicals framework eg haemopoietic progenitor cells (HPC).[1]



The Australian Bone Marrow Donor Registry (ABMDR) is concerned with the ramifications of the above mandatory requirement and would like to draw the TGA's attention to some of the potential barriers that these requirements will impose on providing treatment to Australian patients generally but in particular, the area of import and export. This is particularly relevant in the allogeneic, unrelated donor and transplant area. This includes HPC(A), HPC(M) and HPC(CB) although cord blood will be the subject of an additional, separate submission by the AusCord banks.

At a previous consultation with TGA when the framework was initially being developed we were told that TGA had no intention of implementing regulations which would in any way impose barriers, either physically or administratively to the immediate import or export of HPC.

Both the requirements of the Therapeutic Goods Order (TGO) to minimise infectious diseases and the Draft code of good manufacturing practice impose requirements on manufacturers to comply. However there is an assumption with this approach that all products are manufactured in Australia.

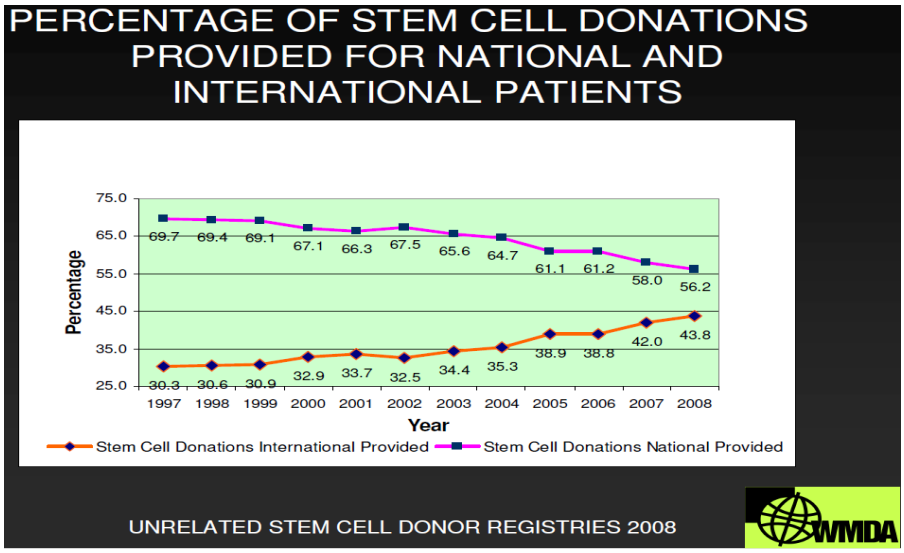
2. Australian patients rely on a global network of donors and cord blood units

There are currently seventy one (71) registries worldwide providing 13.7 million donors and 128 cord blood banks providing 410,000 cord blood units. Fifty one (51) countries with 1,033 transplant centres access these donors and cords. 44% of the HPC transplants that take place worldwide are using international products.

Just over 54% of unrelated allogeneic donations for Australian patients are from international donors.

[1] Guide to consultation process| December 2009| Australian Government Department of Health and Ageing Therapeutic Goods Administration

Transplant centres also act as collection centres so it would be unrealistic and unmanageable to require over 1000 international collection centres to be licensed with the TGA.



Eligibility requirements for donors who have resided/ travelled outside Australia and products manufactured from donors who have lived in the UK in the period between 1980 and 1996, would effectively cease donations from the Anthony Nolan Trust, British Bone Marrow Registry and the Welsh Bone Marrow Donor Registry.

Likewise the requirement that "*... at a minimum be consistent with the policy applied to donors of blood for blood components*" would severely restrict potential donors from donation in Australia, as well as worldwide - donors that could have been a first choice donor for a patient would be excluded before being recruited to the registry. ABMDR and the TGA have had this discussion previously and TGA have acknowledged the need for a risk-benefit approach.

We wish to emphasise that it is imperative that an individual risk-benefit approach to regulation of this area is implemented, one that poses no further barriers to a therapy which provides the only solution to thousands of people each year across the world. The vast majority of patients considering haemopoietic stem cell transplantation face untreated mortality rates in the region of 100% by one year. In this context, risks of even 1 in 1,000 of sudden death, let alone 1 in 1,000,000 of possible transmission of a chronic infectious disease, are irrelevant to their decision making if the best particular HLA matched product is available.

3. Exceptional release

We understand that TGA propose that a mechanism for 'exceptional release' be developed to enable the "*discretionary use of an approved tissue or cellular product which does not conform to manufacturing requirements, standards or release specifications, to be used for an individual patient in unique and critical circumstances.*"

The volume of administration required to manage exceptional releases for any imported donors and cords and the majority of ABMDR donors will be considerable both for the TGA and the suppliers and recipients of all donors and cord blood units (whether international or Australian). All parties will be asked to respond quickly and the

number of requests for exceptional releases will be far greater than the current situation with an occasional cord blood exceptional release.

4. Need for international harmonisation and/or acceptance of equivalent standards

In the past TGA has expressed a desire for international harmonisation of regulatory requirements.

We have been working hard with our colleagues around the world to collaborate through the creation of the Alliance for Harmonisation of Cellular Therapy Accreditation (AHCTA) and the Worldwide Network for Blood and Marrow Transplantation (WBMT).

AHCTA comprises membership of AABB, ASBMT, EFI, EBMT, FACT, ISCT, JACIE, EBMT and WMDA. Its goals are to "harmonise accreditation requirements worldwide by developing core standards for haemopoietic progenitor cells (HPC) which are globally applicable and practicable" and to coordinate efforts with the World Health Organisation (WHO) which in turn is charged with developing "key safety requirements for essential minimally processed human cells and tissues for transplantation."

The ABMDR is an accredited registry with the World Marrow Donor Association and as such requires all entities working on our behalf to meet the WMDA standards with recruitment, selection, testing, collection and transport. Each centre must be fully accredited every five years with an annual self evaluation accreditation provided annually.

We would like to emphasis again, that Australian patients with rapidly fatal haematological malignancies and other severe diseases rely on have prompt access to international HPC and therefore highlighting the importance of an efficient and very timely exchange of HPC between countries. ABMDR is deeply concerned that the current TGA approach to HPC must have a much more explicit definition of the issues relevant to the import of products for Australian patients.

Appendix A. Abbreviations and Definitions

Word	Abbreviation/Definition
AABB	American Association of Blood Banks
ASBMT	American Society for Blood and Marrow Transplantation
EFI	European Federation of Immunology
EBMT	European Bone Marrow Transplant Group
FACT	Foundation for the Accreditation of Cellular Therapy
ISCT	International Society for Cellular Therapy
JACIE	Joint Accreditation Committee of ISCT and EBMT
WMDA	World Marrow Donor Association

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