EXPLANATORY STATEMENT

Subject: THERAPEUTIC GOODS ORDER NO. 88 – *STANDARDS FOR DONOR SELECTION, TESTING AND MINIMISING INFECTIOUS DISEASE TRANSMISSION VIA THERAPEUTIC GOODS THAT ARE HUMAN BLOOD AND BLOOD COMPONENTS, HUMAN TISSUES AND HUMAN CELLULAR THERAPY PRODUCTS.*

Section 10, Therapeutic Goods Act 1989

OUTLINE

Therapeutic Goods Order No. 88 *Standards for donor selection, testing and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products* (TGO 88) is an Order made by the Minister under section 10 of the *Therapeutic Goods Act 1989* (the Act).

TGO 88 specifies a number of important requirements relating to donor selection, donor testing and cell and tissue management, as related to infectious agents during the collection and processing for human blood, blood components, tissues and cellular therapy products and associated critical materials, and also requires that critical materials containing any components of human or animal origin must be assessed in accordance with current TGA policy documents for evaluating risk of transmissible spongiform encephalopathy (TSE).

TGO 88 commenced on 31 May 2013, but a 12 month transition period applies before human blood, blood components, tissues and cellular therapy products must comply with the Order.

Sponsors and manufacturers of human blood, blood components, tissues and cellular therapy products who wish to do so can begin complying with TGO 88 before the 12 month transition period ends (the end of that period being the 31 May 2014).

However, if sponsors and manufacturers wish to begin complying with TGO 88 before 31 May 2014, they must also ensure that the revised *Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapy products (2013)* (the 2013 Code of GMP) is or has been observed in the manufacture of their goods, as these are intended to apply together.

The transition arrangements in TGO 88 recognise that there are blood, blood components, tissues and cellular therapy products that will have been collected prior to the commencement of TGO 88 where the products are in storage. For these products, donor testing requirements (consistent with the previous testing requirements) are specified. In addition there is provision for circumstances where the donor sample for these stored products may not be sufficient to undertake additional testing. If a sponsor wishes to use the product, such as in cases of urgent clinical need, release of the product would be subject to the sponsor performing a risk analysis and seeking agreement from the TGA.

The 2013 Code of GMP commenced at the same time as TGO 88.

BACKGROUND

The Act provides for the establishment and maintenance of a national system of controls relating to the quality, safety, efficacy and timely availability of therapeutic goods for use in

humans. The Therapeutic Goods Administration (TGA) is responsible for administering the Act.

Section 10 of the Act authorises the Minister, or the Minister's delegate, to determine standards for therapeutic goods, or to amend or revoke existing standards, after consultation with the Therapeutic Goods Committee (TGC), a committee established under the Regulations to advise the Minister on matters relating to standards.

TGO 88 is a new standard made under section 10 of the Act, and applies to human blood and blood components (including red cells, white cells, platelets, plasma for infusion and plasma for fractionation), human tissues (such as skin and ocular tissue) and human cellular therapy products (including haematopoietic progenitor cells), collected from living and deceased human donors.

Unless consent is granted by the Secretary under section 14 and 14A of the Act, therapeutic goods imported into Australia, supplied in Australia or exported from Australia must comply with applicable standards.

Under paragraph 32DE(1)(c) of the Act, one of the matters that the Secretary must consider when evaluating an application for inclusion in the Register in relation to a biological (other than a Class 1 biological) is whether the biological conforms to any standards applicable to it.

In addition, one of the bases upon which a biological may be cancelled from the Register under section 32GC of the Act is if the biological does not conform to an applicable standard (paragraph 32GC(1)(f) refers).

TGO 88 is intended to apply in conjunction with the revised *Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapy products (2013)* (the 2013 Code of GMP). TGO 88 includes donor infectious disease screening requirements that have been removed from the previous *Code of Good Manufacturing Practice for Human Blood and Tissues, August 2000* (the 2000 Code of GMP). To minimise potential overlap in requirements (which may result in regulatory burden for manufacturers of blood, cell and tissue products supplied in Australia) and ensure consistency with existing requirements, manufacturers must implement the 2013 Code of GMP and TGO 88 simultaneously.

Unless exempt from the requirements of Part 3-3 of the Act (under Schedule 7 or 8 of the Therapeutic Goods Regulations 1990 (the Regulations)), a manufacturer of human blood and blood components, human tissues and human cellular therapy products must, in addition to implementing the requirements of TGO 88, also comply with the 2013 Code of GMP in relation to their manufacture of such goods.

The requirements of the 2000 Code of GMP have been updated in:

- Code of Good Manufacturing Practice for Human Blood and Blood Components, Human Tissues and Human Cellular Therapy products (May 2013), and
- Therapeutic Goods Order 88: Standards for donor selection, testing and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products.

TGO 88 specifies the minimum donor screening and testing requirements considered necessary for the safety of human blood, cell and tissue products. TGO 88 also includes donor testing criteria and specifies requirements to minimise the risk of contamination of these products during manufacture, such as processing timeframes and transport conditions.

TGO 88 applies to living and deceased donors of products for allogeneic (non-self) use and, where applicable, autologous (self) use. Throughout TGO 88 clauses provide specific criteria for products that are for autologous use where the requirements applicable to products for allogeneic use may not be relevant or appropriate.

TGO 88 provides that the following products are not required to comply with the Order:

- fresh viable human organs, or parts of human organs and associated cells and tissue for direct donor to host transplantation – this is consistent with the current Australian government position that organ transplantation (such as heart or kidney transplantation) is not regulated by the TGA;
- samples of cells or tissue for diagnostic (non-therapeutic) purposes - for example, a vial of blood collected for diagnostic purposes which is not for use in a recipient; and
- blood and haematopoietic progenitor cells that are collected or manufactured by a medical practitioner for a specific patient in the course of clinical practice.

TGO 88 requires that donor medical and social history be obtained before the use of any relevant products collected from the donor. This is important in order to be able to effectively assess the risk of infectious disease transmission associated with the use of blood or blood components, human tissues or human cellular therapy products from the donor. In some cases, a donor will need to be deferred for a period of time before products can be collected from that donor - for example, a donor known to have hepatitis C would be permanently ineligible to donate, whereas a donor suspected of having hepatitis C would be deferred from donating until determined otherwise.

TGO 88 also specifies the minimum physical assessment and testing that must be undertaken to evaluate donor suitability. It is required that this testing is performed using specific technologies that are the most current and effective available methods. Specific requirements are set out in order to address circumstances that are unique to certain blood, tissue and cellular therapy products. For example, where a newborn infant that is a donor (for example a cord blood donor) may be at risk of carrying an infectious disease borne by the mother, the Order requires that the mother must also be evaluated and tested for infectious disease.

TGO 88 includes requirements for microbial control, in order to minimise the risk of introducing microbial contamination in blood, blood component, tissue or cellular therapy product during collection, processing or transport. This includes temperature control to minimise growth of potential contaminants, and testing for microbiological contamination during manufacture and prior to supply of the product.

TGO 88 also specifies requirements for critical materials and substances used in the manufacture of blood, cell and tissue products that come into direct contact with the product and therefore pose a risk to product safety. For example, a cellular therapy product may be expanded/ grown through incubation within a specific solution.

CONSULTATION

A draft of TGO 88 was made available by the TGA for public consultation in December 2009. A substantially revised version, which took into account feedback received regarding the first draft, was published by the TGA in December 2010 for a second round of public consultation. Also in December 2010, the TGA undertook targeted consultation in relation to TGO 88 with several key industry organisations to discuss details of the proposed standard. These bodies included the Australasian Tissue and Biotherapeutics Forum (ATBF), the Australian Red Cross Blood Service (ARCBS) and CSL.

In addition, TGO 88 has been considered and endorsed by the Therapeutic Goods Committee (the TGC) and by a subcommittee of the TGC dealing with biologicals.

REGULATION IMPACT STATEMENT

The TGA prepared a (single) Regulation Impact Statement (RIS) in relation to TGO 88 and the 2013 Code of GMP, and this was approved by the Office of Best Practice Regulation in January 2013 (OBPR ref 12594). A copy of the RIS is attached as Supporting Material.

In relation to compatibility with human rights, it is considered that the TGO 88 is compatible with the human rights and freedoms recognised or declared in the international instruments listed in section 3 of the *Human Rights (Parliamentary Scrutiny) Act 2011*, and a Statement of Compatibility setting that out in further detail is attached as Supporting Material.

SUPPORTING MATERIAL

1. Regulation Impact Statement (RIS) for *revision of manufacturing and technical standard requirements for human blood, human blood components, human tissues and human cell therapy products (2013)*; and

2. Statement of compatibility for a legislative instrument that does not raise any human rights issues (Therapeutic Goods Order No. 88 *Standards for donor selection, testing and minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products*).