Australian Government

Department of Health and Ageing

Therapeutic Goods Administration

Information paper

Consultation on proposed standards for human blood and blood components, human tissues and human cellular therapy products

December 2010

Introduction

The *Therapeutic Goods Amendment (2009 Measures No. 3) Act 2010* (No. 53, 2010) amending the *Therapeutic Goods Act 1989* (the Act), received Royal Assent on 31 May 2010. The amendments in Schedule 1 of the amending Act create a new regulatory framework for a type of therapeutic good known as a biological.

The amendments to the Act to implement the new Biologicals Framework will commence on 31 May 2011, the same day as the amendments to the associated regulations and other legislative instruments, to enable all elements of the new framework to commence together.

The legislative instruments that specify requirements of therapeutic goods include Therapeutic Goods Orders, which mandate product standards and other technical product requirements, and Manufacturing Principles which mandate the Code of Good Manufacturing Practice (Code of GMP) and other manufacturing requirements.

Compliance with relevant standards must be demonstrated as part of the evidence that human cell and tissue therapy products comply with the regulatory requirements. For biologicals in class 2, 3 or 4, compliance with standards will be demonstrated in a dossier. For blood, blood components and haematopoietic progenitor cells, compliance is demonstrated through a technical master file or plasma master file (unless exempt). Compliance with the Code of GMP is demonstrated by successful audit of a manufacturing facility (GMP licence) where required.

Background

The current Code of GMP for Blood and Tissues (2000) applies to blood, blood components, cells, and tissues. The current Code will be replaced by:

1. the proposed new *Code of GMP for human blood and blood components, human tissues and human cellular therapies;* and
2. the *Standards for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapies* (ID Order).

The new Code of GMP and ID Order will come into effect simultaneously.

Product-specific Orders will support the products in the Biologicals Framework and it is anticipated these will be implemented at the time of commencement of the Biologicals Framework.

From 9 December 2009 to 12 February 2010, the following documents were made available for public consultation:

- Australian Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapies
- Standards for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapies, and

four product-specific Therapeutic Goods Orders:

- Standards for banked human cardiovascular tissue
- Standards for banked human musculoskeletal tissue
- Standards for banked human ocular tissue

- Standards for banked human skin.

At the close of consultation, submissions had been received from 42 organisations. Table 1 below indicates the number of submissions received for each of the consultation documents. All original submissions received during consultation period are available for viewing on the TGA website.

Table 1: Responses received from December 2009 consultation on standards and Code of GMP

Consultation document	Number of submissions
Infectious Diseases Order	41
Code of GMP	30
Musculoskeletal Order	12
Ocular Order	6
Cardiovascular Order	5
Skin Order	4

Review of stakeholder feedback

Following close of consultation, each submission was reviewed and summarised into issues for consideration. All comments were considered by relevant TGA experts and initial recommendations or further actions (including research or further stakeholder engagement) were documented. Recommendations fell into two broad groups:

- Accept/Note, resulting in update or modification to a standard and/or noting for inclusion in a guidance document; or
- Reject, resulting in no further action and/or noting for clarification to be included in a Guidance document.

Key issues from previous consultation

Several common areas of stakeholder concern were identified in the feedback from consultation, including:

- Donor selection issues including:
  - Timing and requirements for the examination and consent of living donors;
  - Disease and age exclusion criteria for living donors;
  - Timing and requirements for sampling and testing of donors;
- Assessment of microbial contamination and minimisation of bioburden;
- Requirements for transport, storage, quarantine and banking;
- Standards for plasma for fractionation products;
- Reproduction of similar labelling requirements for all product-specific Orders.

After consideration of stakeholder issues the standards were revised and reformatted. The revised standards are all substantially different in content and presentation to the previous version.

The outcomes of the review process, including summarised stakeholder comments, unresolved issues, revised standards and recommendations, were presented to the Therapeutic Goods Committee Subcommittee on Biologicals (TGC subcommittee) on 22 July 2010.

Consideration of all feedback and review by the TGC subcommittee resulted in significant revisions to all of the standards. Given the significant changes, the TGC subcommittee agreed for the standards to undergo a second round of stakeholder consultation.

Only minimal revisions have been made to the Code of GMP as a result of this process. The Subcommittee has supported the parallel release of the revised Code of GMP for information only, to support the second round of stakeholder consultation.

Development of labelling requirements for Biologicals

Labelling requirements for human tissues were originally incorporated in Schedule 1 of each of the four proposed product-specific Orders. As a result of stakeholder feedback and the review process described above, the labelling requirements have been consolidated into a single set of general labelling requirements for biologicals.

The new draft *General requirements for the labelling of biologicals* sets out minimum labelling requirements applicable to all biologicals defined within the Biologicals Framework (unless exempt). The standard has been developed by:

- considering stakeholder comments on labelling requirements in the four product- specific Orders (cardiovascular, musculoskeletal, ocular and skin);
- consolidating labelling requirements from the four product-specific Orders;
- harmonising the general labelling requirements for biologicals, where applicable, with those for other therapeutic products;
- harmonising the labelling requirements for biologicals, where possible, with international requirements.

Implementation and transition arrangements

Transition provisions under the Biologicals Framework are outlined in the document titled *Resource guide: Overview of the Biologicals Framework* available on the TGA website.

The transition arrangements for the Biologicals Framework are summarised in Table 2.

Table 2. Transition arrangements for the Biologicals Framework

Status of product	Transition time to meet new requirements *from 31 May 2011*
New biological product	Relevant requirements must be met prior to supply.
Current entry on the ARTG	No transition required – automatic inclusion in ARTG as a biological.
Currently exempt from inclusion on the ARTG with existing GMP licence	3 year transition period to be included on ARTG – application submitted within 18 months may result in an extended transition if required
Current exemption from ARTG inclusion and current exemption from GMP licensing requirement	3 year transition period to be included on ARTG and application for licence to be submitted prior to ARTG application.

Transition arrangements for product-specific Orders

Standards for skin, ocular, cardiovascular and musculoskeletal products have not previously been mandated by the TGA, and as such, compliance with the requirements of the product-specific Orders must be demonstrated at the time of application for inclusion of a product on the ARTG as described in Table 2.

Transition arrangements for ID Order and Code of GMP

The draft ID Order has been developed in conjunction with the revised Code of GMP, and harmonisation of the requirements in these two documents necessitates simultaneous implementation. Transition arrangements for compliance with the Code of GMP and the ID Order will be independent of the Biologicals Framework, although concurrent implementation of the Code of GMP and ID Order will facilitate compliance with the requirements of the framework where applicable.

For manufacturers with a current GMP licence against the current Code of GMP for blood and tissues (2000), a 12 month transition period will be in place for manufacturers to comply with the revised Code of GMP and ID Order. Earlier adoption of the revised Code of GMP and ID Order would be permitted at the licence holder's request.

Guidance document for explanatory information

Rather than incorporate Supplementary Notes into the Orders, it is proposed that the Orders would be accompanied by a guidance document providing explanatory information and a series of questions and answers relating to the practical application of the Orders.

Invitation to comment

Interested parties are invited to provide comment on the following draft Therapeutic Goods Orders:

- *Standards for minimising infectious disease transmission via therapeutic goods that are human blood and blood components, human tissues and human cellular therapy products*;
- *Standards for human cardiovascular tissue*;
- *Standards for human musculoskeletal tissue*;
- *Standards for human ocular tissue*;
- *Standards for human skin;*
- *General requirements for the labelling of biologicals.*

The TGA will be reviewing comments received as they relate to each consultation document. To facilitate this process it would be appreciated if comments could be submitted using the template provided below. Included in this template is a question regarding the regulatory impact of the proposed documents, for which a response is optional. Where possible, relevant data and/or examples to support the views expressed should also be provided.

For information

A revised draft Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapy products sets out the manufacturing requirements and is designed to operate in conjunction with the product standards listed above. The revised draft Code of GMP has been provided for context and stakeholders are advised that this document is supplied as information only:

Submissions

As the consultation period includes the Christmas and New Year holiday, a period of 8 weeks for comment has been provided. Submissions must be received by close of business on **Wednesday 2 February 2011.**

Submissions may be made using the template provided on the TGA website:

- Template for submissions: Standards for human blood and blood components, human tissues and human cellular therapy products

Electronic submissions are preferred and should be emailed to biologicals_consultation@tga.gov.au

Please include 'Standards Consultation' and your organisation in the subject line of the email.

As an alternative, hard copy submissions may be faxed to 02 6203 1291 or mailed to:

Administration Officer
Biological Science Section
Office of Scientific Evaluation
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

Cover sheet

Submissions should include the coversheet provided:

- Consultation submission coversheet: Standards for human blood and blood components, human tissues and human cellular therapy products.

Enquiries

Enquiries should be directed via email to biologicals_consultation@tga.gov.au or by telephone to 02 6232 8443.

What will happen to the submissions?

Submissions will be reviewed by the TGA and placed on the TGA Internet site at www.tga.gov.au.

All submissions received will be placed on the TGA's website, unless marked confidential. Any confidential material contained within your submission should be provided under a separate cover from the remainder of the submission, with each page clearly marked 'IN CONFIDENCE'.

Reasons for a claim to confidentiality must be included in the space provided on the TGA submission coversheet.

For submissions made by individuals, all personal details, other than your name, will be removed from your submission before it is published on the TGA's website.

In addition, a list of parties making submissions will be published. Similarly, if you do not wish to have your name included in this list you must specifically request this in the space provided on the submission coversheet.