TGA THERAPEUTIC GOODS ADMINISTRATION

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Commonwealth Department of Health and Ageing

Therapeutic Goods Committee
22nd Meeting (11 August 2003)

Information for Stakeholders – Report on Meeting

The 22nd Meeting of the Therapeutic Goods Committee (TGC) was held in Conference Room 1, Ground Floor, TGA Building, Narrabundah Lane, Symonston on 11 August 2003, commencing at 10.30 a.m. and closing at 4.20 p.m.

Present

TGC Members:	Professor Stella O'Donnell (Chair) Dr John Ballard Dr Mark Bowden Mr David Clayton Associate Professor Loraine Holley Associate Professor William Rawlinson (by teleconference – part meeting only) Professor Klaus Schindhelm
Observers:	Mr Allan Crosthwaite Ms Christine Cuthbertson
TGA officers:	Ms Julie Emery Dr Albert Farrugia Dr Larry Kelly Ms Rita Maclachlan Dr John McEwen
Secretariat:	Ms Lyn Lewis (Secretary)
Apologies:	Ms Amanda Cornwall Mr Philip Daffy Mr Barry Evers-Buckland

AGENDA AND COMMITTEE ADMINISTRATION

Opening of Meeting – Welcome and Apologies

The Meeting was opened at 10.30 a.m. and Members and Observers were welcomed. Apologies were noted.

Terms of Reference

Members noted the Committee's functions, composition and provisions relating to tenure of office as given in Regulation 34 of *The Therapeutic Goods Regulations 1990*.

Adoption of Agenda

Members noted the agenda and agreed the inclusion of an additional agenda item on which TGA was requested to provide advice. Members adopted the agenda as amended, and agreed to varying the order of consideration as necessary to facilitate the attendance of relevant TGA officers.

Conflict of Interest Declarations

In accordance with the Guidelines on Confidentiality and Conflict of Interest adopted by the Committee at its November 2000 Meeting, Members were reminded to complete the Disclosure of Interest Declaration included in the front of the agenda and provide this to the Chairman.

Members also were reminded that, prior to the commencement of any agenda item in relation to which a potential conflict of interest had been declared, the Chairman's attention should be drawn to this fact. In this event, the remainder of the Committee would need to resolve the extent to which that Member could be allowed to participate in the consideration of the item.

Minutes of the 21st Meeting of TGC

Members noted that the Minutes of the 21st Meeting of the TGC were ratified out-of-session on 21 April 2003 according to the process previously determined by the Committee, and that the *Summary of Key Resolutions* and the subsequent *Information for Stakeholders - Report on Meeting* had been published on the TGA website.

TGC SUBCOMMITTEES

The TGC considered the need for establishment of subcommittees, as permitted by the Therapeutic Goods Regulations 1990, to inquire into and report to the Committee on specific matters within the functions of the Committee.

The TGC also considered and agreed on some general principles governing the membership and operation of TGC subcommittees.

These principles included that:

- Subcommittees will only be established when a specific matter requires consideration, and this would be reflected in the subcommittee's Terms of Reference;
- Subcommittees will be chaired by a TGC member, preferably an expert Member rather than an industry Member. This would avoid any perception of conflict of interest in the subcommittee's recommendations;
- Subcommittees would function more efficiently if composed of a small core of expert members, with industry representatives invited to attend subcommittee meetings as appropriate to the matters under discussion; and
- The TGC would look to drawing in expertise from other TGA advisory committees, thereby increasing the interaction between these expert committees.

Several matters were identified by the TGC as requiring consideration by specialised subcommittees and the following were therefore established:
- Subcommittee on Blood and Tissues;
- Subcommittee on Child-Resistant Packaging; and
- Subcommittee on General Standards for Tablets, Pills and Capsules.

Subcommittee on Blood and Tissues

No subcommittee on blood and tissues had existed previously but an ongoing issue was the development of specific standards for application in Australia for haematopoietic stem cells derived from placental cord blood and sources other than placental cord blood.

In view of the very specialised nature of these products, the TGC agreed to establish a subcommittee to undertake this work. Associate Professor William Rawlinson was appointed as Chair of this subcommittee (TGC member with expertise in microbiology and virology), and a number of experts in the field were nominated for membership.

The TGC resolved that:

RESOLUTION NO. 22/01

1. **The Therapeutic Goods Committee establishes a Subcommittee on Blood and Tissues.**

2. **The Subcommittee is to provide a draft Therapeutic Goods Order specifying standards for:**

   - **Haematopoietic stem cells harvested from placental cord blood; and**

   - **Haematopoietic stem cells harvested from sources other than placental cord blood,**

   for consideration by the Therapeutic Goods Committee at its next Meeting.

3. **The Subcommittee is to be Chaired by Associate Professor Rawlinson and have an appropriate membership drawn from experts in this field.**

Subcommittee on Child-Resistant Packaging

The Committee noted that although a new Therapeutic Goods Order on child-resistant packaging was nearing gazettal, there were new issues that would soon require consideration. These issues related to standards for non-reclosable packaging (blister and foil strips) and the effectiveness of these in preventing access to medicine by children. It was noted that some State health departments and Australian injury prevention centres had expressed concerns over this issue and also that the UK had moved to apply new standards for these forms of packaging when used for a small group of products.

The TGC agreed that a subcommittee should be established to look into these matters and report to the TGC. Associate Professor Holley (TGC member with expertise in biomedical engineering) was appointed as Chair of the Subcommittee and it was agreed that members of the Subcommittee should have expertise in packaging technology or injury prevention / poisons information services. Nominations for membership would be progressed out-of-session.

The TGC therefore resolved:

RESOLUTION NO. 22/02

1. **The Therapeutic Goods Committee establishes a Subcommittee on Child-Resistant Packaging.**

2. **The Subcommittee is to advise the Therapeutic Goods Committee on:**

   - **Forms of child-resistant packaging not covered by the existing Therapeutic Goods Orders;**

   - **The newly introduced British Standard (BS 8404:2001*) Packaging – Child-resistant packaging - Requirements and testing procedures for non-reclosable packages for pharmaceutical products* and other relevant international standards; and**

   - **Issues of concern to injury prevention agencies or health departments related to the child-resistant packaging of therapeutic goods.**

3. **The Subcommittee is to be Chaired by Associate Professor Holley and have an appropriate expert membership.**

MEDICINE LABELLING – TGA LABELLING REVIEW AND PERFORMANCE BASED LABELLING

The TGC considered a proposal from the TGA for amendment of Therapeutic Goods Order No. 69 *General requirements for labels for medicines* (TGO 69) to facilitate the transfer of warning statements from the *Standard for the Uniform Scheduling of Drugs and Poisons*

(SUSDP or Poisons Standard) to the document *Mandatory Advisory Statements for Medicine Labels* (MASML). This document was to be a new TGA publication, linked to TGO 69.

The amendments proposed also sought to add a reference in TGO 69 to the Code of Practice being developed on performance-based labelling of non-prescription medicines. Both actions were outcomes from the recommendations made in the TGA's Consultation Report *Review of Labelling Requirements for Medicines – Consumer-focussed labelling – A Way Forward?* published in March 2002.

The Committee had given in-principle support to the consolidation of warning statements into a single document at its 20th Meeting in April 2002, and had been further briefed on progress with this project at its 21st Meeting in February 2003. The Committee had noted at that time that changes to TGO 69 would be required.

The TGC was advised that the new TGA document, *Mandatory Advisory Statements for Medicine Label*, was under preparation, and industry, consumers and the TGA were all involved in its development. Work also was in progress on the industry Code of Practice that would implement performance-based labelling for non-prescription medicines. While it was not intended that compliance with this Code would be mandatory, the TGA sought to reference it in TGO 69.

The proposed effective date for the changes to TGO 69 was 1 July 2004, which would coincide with the end of the transition period between TGO 69 and its predecessor TGO 48. No transition period was considered necessary as the action would only transfer existing requirements from one regulatory document to another, with no regulatory impact. The TGA intended that associated changes to the *Therapeutic Goods Act 1989* and regulations would occur concurrently.

The TGC noted that the amendments to TGO 69 now proposed related to part only of the labelling considerations being undertaken by the TGA, and that further amendments, including the identification on labels of the manufacturer of the medicine, would need to be considered at a future meeting.

Following discussion of the detail of the proposed amendments to TGO 69, the Committee resolved:

RESOLUTION NO. 22/03

1. **The Therapeutic Goods Committee notes that the new ancillary document, *Mandatory Advisory Statements for Medicine Labels,* will contain the warning statements transferred from the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP), as well as advisory statements from other sources such as the Therapeutic Goods Regulations;**

2. **The Therapeutic Goods Committee recommends the following amendments to Therapeutic Goods Order No. 69 *General requirements for labels for medicines,* and that these amendments be implemented with effect from 1 July 2004:**

- **Amend the definition of 'warning statements' contained in clause 2(1) *Interpretation* of Therapeutic Goods Order No. 69, to read:**

  'warning statements' means:
  (a) any labelling requirements specified in the *Mandatory Advisory Statements for Medicine Labels*;
  (b) any warning statements specified in the standard that applies to the goods;
  (c) a warning statement where incorrect route or method of administration may be hazardous;
  (d) any warnings required by the Secretary, Department of Health and Ageing to be included as a condition of Registration/Listing in relation to the goods;

- **Insert, immediately before clause 1 *Application and exemptions*, the following heading and paragraphs :**

  Introduction

  The purpose of a medicine label is to provide information about the product such as its identity, potency, content, storage, expiry date, registration status and distributor. Medicine labels also include other information not required by the Order, but which may be required by other legislative instruments or for commercial purposes. These include items such as signal headings (eg. prescription only, pharmacist only), bar codes and sponsor's logos.

  For non-prescription medicines, the aim is that the information on the label is presented in such a way that consumers can:

  (a) choose an appropriate medicine on their own;
  (b) use the medicine safely and effectively;
  (c) readily find the information they need, understand it and act on it; and
  (d) access further information, if they want to know more about the medicine.

  Although there may be various means of achieving the aim stated above, products with labels that have been designed in accordance with the industry Code of Practice entitled [*title of the industry code to be inserted*][1] and published by *[publication details to be inserted*][2] will be taken to achieve this aim.

  The mandatory aspects of this Order for all medicines are contained in clauses 1- 7 inclusive and the Schedules to the Order.

1 Expected title is "Designing medicine labels for people – a code of practice for developing usable labels for non-prescription medicines"

2 To be published by the Communication Research Institute of Australia

STANDARDS FOR TAMPER-EVIDENT PACKAGING OF THERAPEUTIC GOODS

The TGC considered the adoption of the document *Code of Practice for the Tamper-Evident Packaging of Therapeutic Goods* as a packaging standard for therapeutic goods in Australia.

This Code of Practice had been developed by the TGA's Industry Government Crisis Management Committee (IGCMC) as part of a package of strategies aimed at preventing, or minimising the effect of product tampering incidents in Australia. The Code of Practice superseded an industry guideline document *Guideline for the Tamper-Evident Packaging of Medicines, Complementary Healthcare Products and Medical Devices* that had been implemented in January 2001 with the intention that it would be enforced through legislation at the end of its three year transition period.

The TGC noted that the IGCMC had undertaken wide stakeholder consultation on the draft Code of Practice and, following this, recommended that the Code of Practice be adopted through a Therapeutic Goods Order as a packaging standard for therapeutic goods in Australia.

Those therapeutic goods falling within the Scope of the Code of Practice were those most likely to be available to consumers for self-selection, or on open display in pharmacies and other retail outlets and, that by virtue of their dosage form or route of administration, presented the greatest opportunity for tampering. Legislative underpinning of the Code of Practice would achieve uniform application to all sponsors of therapeutic goods.

The TGC therefore resolved:

RESOLUTION NO. 22/04

> **The Therapeutic Goods Committee recommends that the publication *Code of Practice for the Tamper-Evident Packaging (TEP) of Therapeutic Goods*[3] be adopted through a Therapeutic Goods Order as a standard in Australia for therapeutic goods, with effect from 1 January 2004 and with a 12-month implementation period from 1 January 2004 for full compliance.**

REVIEW OF THERAPEUTIC GOODS ORDER NO. 56 *GENERAL STANDARD FOR TABLETS, PILLS AND CAPSULES* (TGO 56)

At its 21st Meeting in February 2003, the TGC had considered a submission requesting revision of certain aspects of Therapeutic Goods Order No. 56 *General standard for tablets, pills and capsules* (TGO 56). While the TGC had agreed in principle to some of the requested revisions, the Committee had acknowledged that there were safety issues associated with other of the requested revisions and these needed further consideration. The TGC also noted a number of other parts of TGO 56 were in need of review and, overall, this may result in significant amendment to the Order. The TGC had requested that the TGA canvass

3 Available on the TGA website at http://www.tga.gov.au/docs/html/tepguide.htm

stakeholders to identify those aspects of TGO 56 that were problematic.

The TGC noted responses from stakeholders, as well as advice from TGA regulators identifying those aspects of TGO 56 that were in need of review. Historically, TGO 56 had been developed to specify those requirements that were not addressed adequately in the British Pharmacopoeial (BP) general monographs for tablets and capsules. Although the BP had undergone considerable amendment since TGO 56 had been finalised in 1996, it was apparent that the BP still did not adequately address some matters. The TGC also noted that TGO 56 had been developed mainly in the context of prescription and conventional non-prescription medicines, and while it also applied to complementary medicines, there were aspects of TGO 56 relevant to complementary medicines that were ambiguous or inadequate.

To progress a full review of TGO 56, the TGC agreed to the establishment of a subcommittee, the Subcommittee on General Standards for Tablets, Pills and Capsules. This Subcommittee would be chaired by Professor O'Donnell (TGC Chair and member with expertise in the pharmaceutical sciences). Nominations for membership would be considered out-of-session. The TGC therefore resolved:

RESOLUTION NO. 22/05

1. **The Therapeutic Goods Committee:**

   - **Notes those issues raised by stakeholders in relation to the proposed review of Therapeutic Goods Order No. 56 (TGO 56) *General Standard for Tablets, Pills and Capsules;* and**

   - **Establishes a Subcommittee on General Standards for Tablets, Pills and Capsules to consider those issues in detail and the continued relevance of a general standard for tablets, pills and capsules.**

2. **The Subcommittee is to undertake a review of TGO 56, taking into account:**

   - **Changes in the British Pharmacopoeia since TGO 56 was gazetted;**

   - **Characteristics of, and regulatory arrangements for, prescription, non-prescription and complementary medicines; and**

   - **Relevant international standards,**

   and provide a report to the first meeting of the Therapeutic Goods Committee in 2004.

3. **The Subcommittee is to be Chaired by Professor O'Donnell and have an appropriate expert membership, supplemented with relevant industry representation.**

AMENDMENT TO THERAPEUTIC GOODS ORDER NO. 70 *STANDARDS FOR EXPORT ONLY MEDICINE*

Therapeutic Goods Order No. 70 *Standards for Export Only Medicine* (TGO 70) provides for medicine manufactured in Australia, or imported into Australia, for export only, to be able to comply with any one of a range of alternate pharmacopoeial standards. One of these alternate pharmacopoeial standards was the United States Pharmacopeia 25th edition (USP 25).

The TGC noted that USP 25 had been superseded by the 26th edition (USP 26).

In accordance with the Committee's previous recommendation that TGO 70 should be maintained to reflect the most recent editions of each of the referenced pharmacopoeias, the TGC resolved that:

RESOLUTION NO. 22/06

> **The Therapeutic Goods Committee recommends that Therapeutic Goods Order No. 70 *Standards for Export Only Medicine* be amended to replace the reference to United States Pharmacopeia 25th edition with reference to United States Pharmacopeia 26th edition.**

STANDARD FOR HAEMATOPOIETIC STEM CELL (HSC) PRODUCTS

At its previous Meeting in February 2003, the TGC had been informed that haematopoietic stem cells (HSCs) would not be covered by the next edition of the Council of Europe's *Guide to the Preparation, Use and Quality Assurance of Blood Components,* which was adopted through Therapeutic Goods Order No. 66 *Standards for Blood Components* as the general standard in Australia for blood and blood components. As a consequence of this, there was a need for Australia to identify and adopt a new standard for HSCs.

An expert Advisory Group convened by the TGA to consider options for a new standard for HSCs in Australia, both those harvested from placental cord blood and those harvested from non-cord blood, had recommended the adoption of the following two overseas documents for this purpose:

- *International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection and Release* – 2nd edition, NETCORD and Foundation for the Accreditation of Hematopoietic Cell Therapy (FAHCT) (July 2001), for HSCs harvested from placental cord blood; and

- *Standards for Hematopoietic Progenitor Cell Collection, Processing & Transplantation* – 2nd edition, Foundation for the Accreditation of Cellular Therapy (FACT) (March 2002), for HSCs harvested from sources other than placental cord blood, subject to the inclusion of a preamble to clearly identify the scope of TGA regulation of HSC products and to differentiate this from medical practice and other issues relevant only in the US.

Noting this, the TGC had requested that the TGA consult with NETCORD and Foundation for

the Accreditation of Cellular Therapy (FACT) in the USA on the adoption of these standards under Australian legislation.

At the current Meeting, the TGC was advised that the TGA had held discussions with FACT and although FACT expressed some initial reservations regarding excision of provisions that were inappropriate in the Australian context, these had been resolved. Agreement had consequently been obtained for the adoption of the FACT standard, with the necessary qualifications to clarify which sections were mandatory or non-mandatory in the Australian context. Wording of the proposed qualifications was as follows:

> The Second Edition of the *Standards for Hematopoietic Progenitor Cell Collection, Processing & Transplantation* of the Foundation for the Accreditation of Cellular Therapy is the Australian Standard for haemopoietic Stem Cells harvested from sources other than placental cord blood.
>
> *The provisions of this document shall apply to those areas of haemopoietic stem cells related to product quality and quality system management. Areas in the document related to medical practice, organisational structure, personnel qualification and others not directly related to product quality and quality system management are not mandatory. Areas in the document reflecting areas of good manufacturing practice specified in the Australian Code for Good Manufacturing Practice for Human Blood and Tissues shall be subservient to that Code. Areas in the document reflecting the practice of clinical research as specified by the National Health and Medical Research Council shall be subservient to the relevant guidelines of that organisation. Areas in the document relating to the disposal of haemopoietic stems cells addressed by provisions in the relevant legislation of the individual states and territories shall be subservient to those provisions.*
>
> *The TGA will negotiate with individual agencies when areas of possible contention arise.*

In relation to adoption of the recommended standard for cord-blood derived HSCs, the TGC noted that one of the expert members on the Advisory Group had undertaken to facilitate the negotiation with NETCORD. It was anticipated that advice on this would be available for the next meeting of the TGC.

As regards to the adoption of these standards through a Therapeutic Goods Order (TGO), the Committee was advised that some matters were still under discussion between the TGA and the HSC sector. Once a consensus position was reached, the TGA would progress the new TGO for HSCs, with this incorporating the new standards to be applied and also the level of regulation for the various manufacturing environments for these products. It was intended that the TGO would be ready for consideration by the TGC at its next Meeting.

The TGC therefore resolved:

RESOLUTION NO. 22/07

The Therapeutic Goods Committee notes:

- **Progress in the development of a Therapeutic Goods Order as a standard in Australia for haematopoietic stem cells; and**

- **That the draft Therapeutic Goods Order will be referred to the next meeting of the Committee for consideration.**

UPDATE ON MEDICAL DEVICE STANDARDS

The TGC noted an update on adoption of medical device standards under the new medical devices regulatory system.

It was reported that since the 18th Meeting, the TGA had worked extensively with Standards Australia International (SAI) to adopt a number of ISO, IEC, CEN or CENELEC standards as Australian Standards. This had occurred in two stages to date, with a third stage in progress. In total 80 standards had been published by SAI as Australian Standards. A number of other standards were still under consideration by SAI.

Concurrently, the TGA had developed a set of Medical Device Standards Orders (MDSO) and Conformity Assessment Standards Orders (CASO) to underpin the requirements of the legislation. The Orders published to date were:

- Medical Device Standards for Clinical Evidence;
- Medical Device Standards for Risk Management;
- Medical Device Standards for Medical Devices Required to be Sterile;
- Conformity Assessment Standard for Quality Management Systems and Quality Assurance Techniques; and
- Conformity Assessment Standards for Quality Assurance Techniques for Animal Tissues and their Derivatives utilised in the Manufacture of Medical Devices.

Further Orders were under development for:
- Electromedical Devices;
- Dental materials implants and instruments;
- Sterilants and Disinfectants; and
- Biological safety.

The TGC noted that, although compliance with these Australian Standards was not mandatory, they provided guidance to manufacturers and were regarded as the simplest way for a manufacturer to demonstrate compliance with the Essential Principles of quality, safety and performance. The TGC resolved:

RESOLUTION NO. 22/08

The Therapeutic Goods Committee notes:

- **The Medical Device Standards Orders[4] and Conformity Assessment Standards Orders[5] gazetted to date; and**

- **Those EN, ISO and IEC standards on medical devices adopted as Australian Standards[6] by Standards Australia.**

OTHER MATTERS

Review of the *Code of Good Wholesaling Practice for Therapeutic Goods for Human Use*

At its 21st Meeting in February 2003, the TGC established a Working Party to progress a review of the document *Code of Good Wholesaling Practice for Therapeutic Goods for Human Use* (cGWP). The TGC had been requested to undertake this review by the National Coordinating Committee on Therapeutic Goods.

The Working Party, which included representation from each of the four key industry associations, wholesalers of therapeutic goods and State Health Departments, was being chaired by Professor O'Donnell. The TGA participated in an advisory capacity.

The TGC was advised that the first meeting of the Working Party had been held on Wednesday 30 July 2003, and noted a report from the Chair of the Working Party. This meeting had explored a number of issues in relation to the Code, many of which were complex, but the meeting had made significant progress.

The TGC noted the Working Party's intended work-plan to progress the revision of the Code prior to it being circulated for consultation.

The Pan Pharmaceuticals Recall

The TGC noted a verbal report on the recent recall of a large number of products manufactured by Pan Pharmaceuticals Limited associated with the suspension of the company's manufacturing licence.

Trans-Tasman Therapeutic Goods Agency

The Committee received a briefing from the TGA's Trans-Tasman Group on progress towards the establishment of a joint regulatory agency for therapeutic products.

Harmonisation of Australian Approved Names (AAN) with International Non-Proprietary Names (INN)

The TGC was provided with a progress report on this action, which had previously been recommended by the Committee. It was noted that:

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4 Available on TGA website at http://www.tga.gov.au/docs/html/devstdord.htm
5 Available on TGA website at http://www.tga.gov.au/docs/html/castdord.htm

6 See Attachments 1 and 2

- With respect to new substances, the TGA had been for some time routinely adopting the INN (where one existed) as the AAN;
- For existing substances, the TGA had been awaiting finalisation of BP position. This had recently been released, with the timing of name changes in the UK to coincide with the date that BP 2003 comes into force in the UK. There would be no change to a few of the more problematic names including adrenaline; and
- The issue of naming was relevant to the Trans-Tasman harmonisation process; and
- The TGA would now progress the matter through TGC at its next Meeting.

CLOSE OF MEETING

The TGC noted that its next meeting would be held in November 2003, with a date to be determined out-of-session[7].

The Chair closed the Meeting at 4.30 pm and thanked Members for their attendance.

The Minutes of the 22nd TGC Meeting were signed by the Chair on 6 November 2003 as a true and correct record of the Meeting.

7 Date for 23rd TGC Meeting subsequently scheduled for 19 November 2003