Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Therapeutic Goods Committee

30TH MEETING (3 MAY 2007)

INFORMATION FOR STAKEHOLDERS – REPORT ON MEETING

The 30th Meeting of the Therapeutic Goods Committee (TGC) was held by teleconference on 3 May 2007, commencing at 10.00 a.m. and closing at 11.20 a.m.

Participating

TGC Members:

Professor Stella O'Donnell (Chairperson)
Dr John Ballard
Dr Mark Bowden
Mr David Clayton
Mr Philip Daffy
Mr Barry Evers-Buckland
Professor Klaus Schindhelm
Mr John Stubbs

Apologies:

A/Professor Loraine Holley
Professor William Rawlinson

TGA officers:

Mr Benjamin Battisson (part meeting)
Dr Albert Farrugia (part meeting)
Mr Tony Gould (part meeting)
Dr Frank Hoeren (part meeting)
Dr Larry Kelly
Ms Siepie Larkin (part meeting)

Secretariat:

Ms Lyn Lewis (Secretary)

AGENDA AND COMMITTEE ADMINISTRATION

WELCOME AND APOLOGIES

The Chairperson opened to Meeting at 10.05am and welcomed Members. Apologies were noted.

The Chairperson also welcomed TGA staff to the Meeting, noting that various officers would attend for items as relevant.

TERMS OF REFERENCE AND MEMBERS' CONTACT DETAILS

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.*

Members were requested to check their contact details as currently held by the Secretariat and to advise of any errors or changes.

ADOPTION OF AGENDA

The Committee adopted the agenda, with some variation to the order of consideration of items.

CONFLICT OF INTEREST DECLARATIONS

Members were reminded of the requirement for submission of Disclosure of Interest Declarations, and the verbal declaration of any potential conflicts of interest.

There were no conflicts of interest relevant to the Meeting.

MINUTES OF THE 29TH MEETING OF THE TGC

The TGC noted that, in accordance with usual practice, the Resolutions and Minutes of the 29th TGC Meeting held on 7 September 2006 were ratified out-of-session and the key resolutions and a report for stakeholders were published on the TGA website.

RESOLUTION:

THE THERAPEUTIC GOODS COMMITTEE NOTES THAT:

- **THE MINUTES OF THE 29TH MEETING OF THE THERAPEUTIC GOODS COMMITTEE HELD ON 7 SEPTEMBER 2006, WERE RATIFIED OUT-OF-SESSION AS A TRUE AND ACCURATE RECORD OF THAT MEETING; AND**
- **THE DOCUMENTS *SUMMARY OF KEY RESOLUTIONS* AND *INFORMATION FOR STAKEHOLDERS – REPORT ON MEETING* HAVE BEEN PUBLISHED ON THE TGA WEBSITE.**

ACTIONS ARISING FROM THE 29TH MEETING OF THE TGC

The TGC received a report on the status of actions arising from the 29th TGC meeting. All requested actions had been completed and some items were reflected in the agenda of the current Meeting.

The Committee noted that:

- the draft ANZTPA Order on child-resistant packaging, developed by the TGC's Subcommittee on Child-Resistant Packaging, had been progressed through the Joint Interim Expert Advisory Committee on Standards (JIEACS) and was undergoing final drafting checks;
- An amendment to TGO 70 relating to export-only medicines had been published, in accordance with TGC's recommendation that the editions of pharmacopoeia referenced in this Order be updated; and
- Further revision to the draft *Code of Good Wholesaling Practice for Therapeutic Goods for Human Use* was being undertaken by the National Coordinating Committee on Therapeutic Goods (NCCTG).

SUMMARY AND STATUS OF THERAPEUTIC GOODS ORDERS

The TGC noted the summary of current and revoked Therapeutic Goods Orders included as a standing item in the agenda. A number of Orders previously recommended by the Committee for revocation would cease to have effect on 1 January 2008 through their non-inclusion on the Federal Register of Legislative Instruments.

MEDICINAL PRODUCTS

ADOPTION OF BRITISH PHARMACOPOEIA 2007

The TGC was requested to consider, and make a recommendation concerning, the adoption of British Pharmacopoeia 2007 (BP 2007) as the edition of that document defined under the *Therapeutic Goods Act 1989* (the Act). The British Pharmacopoeia (BP) was the principal (or default) standard applying, under the Act, to medicines.

The TGC noted that the BP was published annually and, since 1 July 2006, British Pharmacopoeia 2005 (BP 2005) has had effect in Australia. Adoption of new editions on a date as close as practical to the date on which the publication becomes effective in the United Kingdom helped to maintain consistency with international standards for the quality and safety of therapeutic goods and allowed for the timely update of technical matters such as analytical methods.

As BP 2007 became effective in the UK on 1 January 2007, the TGA had undertaken consultation with stakeholders on the adoption of this edition of the BP as the edition defined under the Act. In particular, the TGA had sought comment on any particular difficulties for sponsors that may be associated with the adoption of BP 2007. The TGA also sought information on business compliance costs and impacts on business and individuals, including restrictions on competition, so that a preliminary assessment of the regulatory impact of the proposal to adopt BP 2007 could be undertaken. Comment was also sought on the costs and other consequences that may be associated with not amending the definition as proposed.

The TGC was advised that, in past years, adoption of new editions of the BP had been a fairly mechanical process although a small number of comments regarding the frequency of new editions and potential compliance costs were usually noted. A complication this year was the proposal that, under ANZTPA, the United States Pharmacopeia (USP) and the European Pharmacopoeia (PhEur) would be equally acceptable to the BP as default standards. For this reason, XXXXX had proposed not adopting BP 2007 but waiting for the commencement of ANZTPA when sponsors could choose between the three pharmacopoeias. In contrast however XXXXX had no objections to adoption of BP 2007 and XXXXX considered that adopting BP 2007 as quickly as feasible would be appropriate.

The TGA regulators uniformly supported adoption of the most recent standards and it was considered that, in principle, the TGA should maintain currency with international standards. Many of the changes were relatively minor, but may include improvements in methodology or controls over impurities, or added substances not covered in previous editions. They therefore reflected improvements in quality.

The TGC noted advice that the adoption of BP 2007 had been discussed at a recent meeting of XXXXX. This meeting had considered some of the issues raised by XXXXX in its response, and it became apparent that some of the comments made in that response reflected misunderstandings. With regard to purity levels for one particular substance named, that meeting noted that, as with all Orders, a mechanism existed to permit exemptions where justified. Therefore BP 2007 could be adopted, with specific difficulties such as that for the named substance being addressed on case by case basis.

The TGC also noted that, although ANZTPA was well underway, as yet there was no definite date for commencement of the joint regulatory scheme. Until such time as the joint scheme commenced existing legislative arrangements persisted, and any unforeseen delays to commencement, together with the transition period for products to gain a joint agency licence, could result in BP 2005 (if not updated) remaining in force for some products for a considerable length of time.

As adoption of BP 2007 was considered appropriate from the regulatory perspective, and there was general support from industry for moving to BP 2007, the TGC recommended that BP 2007 should become effective in Australia on 1 July 2007.

In relation to the issue of compliance costs associated with updating documents to reflect new editions of the BP, as raised by one stakeholder, it was suggested that reference in specifications to the BP (or other pharmacopoeia as relevant) without the edition being stated should be adequate to convey that the current edition applied. The exception to this would be when the monograph used was not from the current edition. The meeting noted that in practice however GMP auditors may expect company documents to state the edition of the pharmacopoeia referenced. It was recommended therefore that this matter be taken up with the Manufacturer Assessment Branch (MAB) so that a uniform approach could be taken and a consistent message provided to industry.

RESOLUTION:

THE THERAPEUTIC GOODS COMMITTEE RECOMMENDS THE ADOPTION OF THE BRITISH PHARMACOPOEIA 2007 ON 1 JULY 2007 FOR THE PURPOSES OF THE EDITION OF THE BRITISH PHARMACOPOEIA DEFINED UNDER THE *THERAPEUTIC GOODS ACT 1989*.

UPDATE TO THE AUSTRALIAN CODE OF GOOD MANUFACTURING PRACTICE FOR MEDICINES

The TGC was advised of the intention of the TGA and Medsafe to consult with industry stakeholders on a proposed update to the Australian *Code of Good Manufacturing Practice for Medicinal Products* (the Code) to reflect current international regulatory practices.

It was noted that the current Australian Code was published in August 2002, and was based on the version of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) *Guide to Good Manufacturing Practice for Medicinal Products* current at the time. Since then, the PIC/S Guide had been revised five times, the current version being dated 1 August 2006. The NZ *Code of Good Manufacturing Practice for Manufacture and Distribution of Therapeutic Goods* had not been updated since the early 1990s.

The TGC was informed that the revised document would be a joint Australia NZ Code and the TGA and Medsafe intended to implement it at the commencement of ANZTPA. It would therefore be consulted on widely in both Australia and NZ as a draft ANZTPA document.

RESOLUTION:

THE THERAPEUTIC GOODS COMMITTEE NOTES THE INTENTION OF THE THERAPEUTIC GOODS ADMINISTRATION AND MEDSAFE TO CONSULT WITH THE REGULATED INDUSTRY IN RELATION TO UPDATING THE *CODE OF GOOD MANUFACTURING PRACTICE FOR MEDICINAL PRODUCTS* TO REFLECT CURRENT INTERNATIONAL REGULATORY PRACTICES.

BLOOD AND TISSUES

UPDATE ON STANDARDS FOR CORD BLOOD BANKING

This agenda item advised the TGC of the publication, in December 2006, of the 3rd edition of the Netcord and the Foundation for the Accreditation of Cellular Therapy (Netcord-FACT) document *International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection, and Release* and sought a recommendation from the TGC on whether this edition should be adopted in Australia as the required standard for cord blood banking. If so, it would replace the previous edition of the same publication which had been adopted by the TGA in 2005 following TGC consideration.

The TGC noted the background to the adoption, in Australia, of standards for haematopoietic progenitor cells (HPCs) derived from cord blood, initially those of the Council of Europe (CoE) document *Guide to the preparation, use and quality assurance of blood components* 8th edition (the Guide) as described in Therapeutic Goods Order No. 66 and No. 66A *Standards for Blood Components*, and more recently those of the Netcord-FACT document *International Standards for Cord Blood Collection, Processing, Testing, Banking, Selection and Release* (2nd edition, July 2001), as described in Therapeutic Goods Order No. 73 *Standards for haematopoietic progenitor cells derived from cord blood* (TGO 73).

The TGC now was advised that the TGA had reviewed the 3rd edition of the Netcord-FACT document, and that the new edition introduced changes that would have no significant operational or cost impact on the cord blood banking industry in Australia. The key points of difference were:

- Reorganisation of some chapters to consolidate quality management issues;
- Inclusion of a new clause stating that maternal blood samples obtained between seven days before or after collection of the cord should test negative (D16.4) for Human Immunodeficiency Virus I/II, Hepatitis B surface antigen, Hepatitis C, Human T cell lymphotropic virus I/II (noting however that TGO 73 *Standards for haematopoietic progenitor cells derived from cord blood* and the *Australian Code of Good Manufacturing Practice Human Blood and Tissues* currently required negative serology tests for these pathogens except under specified conditions, and therefore the intent of this new clause was already in place in Australia and did not represent a new impost); and
- Clarification of the test response for *Treponema pallidum* to broaden donor eligibility. This, in conjunction with proposed changes to the cGMP currently in consultation would provide more flexibility with the potential to increase the number of eligible cord blood donors and be a significant step in the building of a cord blood resource for the Australian indigenous population.

The new edition also differentiated more logically between requirements for autologous and allogeneic cord blood units. No other changes to the regulation of HPCs derived from cord blood were proposed. The requirements for cord blood manufacturers to hold a manufacturing licence, to comply with Good Manufacturing Practice and submit a Technical Master File would stand, as would the blood testing requirement described in Item 2 of TGO 73.

The TGC was informed that the proposed new standard had been discussed with public and private cord blood banks and representatives of the Department of Health and Ageing at meetings convened by the TGA in late 2006 and the written comment on the proposal to adopt the 3rd edition of the Netcord-FACT publication as the regulatory standard for cord blood banking had been invited.

Support for the proposal had been provided by XXXXX, which noted that the new standards were substantially the same as the previous standards applied to cord blood, but strengthened the previous version, provided greater detail regarding compliance and provided a detailed focus on collection of cord blood for family and individual donation. The proposed new standards were not likely to have any significant additional direct or indirect impact on the cord blood sector but would ensure that Australia's regulation of HPC-cord blood remained internationally consistent.

XXXXX had responded to the invitation to comment and generally had been in agreement with adoption of the standards given an adequate implementing period. The majority of the comments related to issues that were already subject to regulation through the previously agreed standards.

In relation to implementation, the TGC was advised that although the differences between the 2nd and 3rd editions of the Netcord-FACT publication were not significant, some points may require clarification and updating in the Technical Master Files. The TGA therefore proposed an implementation period of six months from the date of gazettal.

After seeking clarification of the extent of the consultation undertaken, and noting the importance of remaining consistent with international requirements, the TGC resolved as follows.

RESOLUTION:

THE THERAPEUTIC GOODS COMMITTEE:

1. **NOTES THAT:**
   - **THE THERAPEUTIC GOODS ADMINISTRATION (TGA) HAS CONSULTED WITH STAKEHOLDERS ON THE ADOPTION OF THE NETCORD AND FOUNDATION FOR THE ACCREDITATION OF CELLULAR THERAPY (NETCORD-FACT) DOCUMENT *INTERNATIONAL STANDARDS FOR CORD BLOOD COLLECTION, PROCESSING, TESTING, BANKING, SELECTION, AND RELEASE* (3RD EDITION, 2006); AND**
   - **STAKEHOLDERS PROVIDED OVERALL SUPPORT FOR THE ADOPTION, ALTHOUGH REQUIRING CLARIFICATION OF SOME TECHNICAL DETAILS.**
2. **RECOMMENDS THAT THE TGA, UNDER SECTION 10 OF THE *THERAPEUTIC GOODS ACT 1989*, ADOPT THE NETCORD-FACT STANDARD *INTERNATIONAL STANDARDS FOR CORD BLOOD COLLECTION, PROCESSING, TESTING, BANKING, SELECTION, AND RELEASE* (3RD EDITION, 2006) FOR THE REGULATION OF HAEMATOPOIETIC PROGENITOR CELLS DERIVED FROM CORD BLOOD.**
3. **NOTES THAT THE TGA HAS RECEIVED ADVICE ON THE NEED FOR A REGULATION IMPACT STATEMENT FROM THE OFFICE OF BEST PRACTICE REGULATION AND THERE IS NO NEED FOR FURTHER ACTION IN THIS REGARD.**

MEDICAL DEVICES

UPDATE ON REFERENCE IN THERAPEUTIC GOODS ORDERS TO WITHDRAWN OR SUPERSEDED STANDARDS

At its last Meeting, the TGC had considered the currency and continuing relevance of two Therapeutic Goods Orders (TGO 59 *Polymer Urethral Catheters for General Medical Use* and TGO 63 *Standard for Sterile Therapeutic Goods*) and whether either Order required updating.

TGO 59 adopted, with minor amendment, the provisions of the Australia New Zealand Standard AS/NZS 2696:1996 *Medical devices – Polymer urethral catheters for general medical use* as the required standards for polymer urethral catheters. Although AS/NZS 2696:1996 had been withdrawn by Standards Australia, the TGC had agreed that this remained the most appropriate standard for polymer urethral catheters until the end of the transition period for the new regulatory scheme for medical devices. The TGC had noted however that the TGA was seeking legal advice as to whether continued reference in a legislative instrument to an Australia New Zealand Standard that had been withdrawn presented any legal difficulties. The TGC requested that it be advised of the outcome of this legal advice.

TGO 63 determined that the requirements specified in British Pharmacopoeia 1998, Appendix XVI – Tests for Sterility [European Pharmacopoeia, Supplement 1998, Biological Tests-Sterility] constituted the standard for therapeutic devices that were labelled as sterile or sterilised or otherwise

purported to be sterile or sterilised. However the edition of the BP current under the *Therapeutic Goods Act 1989*, BP 2005, contained an updated appendix on sterility testing. The TGC had noted technical advice that the differences between BP 1998 and BP 2005 were relatively minor and should not present a problem in taking regulatory action if a sterile device failed the test for sterility conducted in accordance with BP 2005. However the TGA was also seeking legal advice as to whether this approach was sound.

The TGC was now informed of the nature of the legal advice received.

In relation to TGO 59, it appeared there was no legal impedient to the TGA testing medical devices against TGO 59, as it was immaterial from a legal perspective that the Australian Standard incorporated in the Order had been withdrawn by Standards Australia. In relation to TGO 63, again there was no legal impediment to TGA testing a therapeutic device against an international standard even though the international standard has been replaced by an updated version. Furthermore, if regulatory action against a device for failing the BP test was proposed, then the TGA would need to have performed the test according to the version of the standard specified in the Order.

The TGC noted this advice and that the TGA proposed not to update either TGO 59 or TGO 63 so close to the end of the transition period for the new regulatory system for medical devices.

RESOLUTION:

THE THERAPEUTIC GOODS COMMITTEE NOTES THAT:

- **FURTHER TO THE ADVICE PROVIDED BY THE COMMITTEE AT ITS 29TH MEETING, THE THERAPEUTIC GOODS ADMINISTRATION HAS CONFIRMED THAT THERE IS NO LEGAL IMPEDIMENT TO TESTING A THERAPEUTIC DEVICE AGAINST A NATIONAL OR INTERNATIONAL STANDARD REFERENCED IN A THERAPEUTIC GOODS ORDER EVEN THOUGH THAT NATIONAL OR INTERNATIONAL STANDARD HAS BEEN REPLACED BY AN UPDATED VERSION OR WITHDRAWN; AND**
- **AS THERAPEUTIC GOODS ORDER NO. 59 *POLYMER URETHRAL CATHETERS FOR GENERAL MEDICAL USE* (TGO 59) AND THERAPEUTIC GOODS ORDER NO. 63 *STANDARD FOR STERILE THERAPEUTIC GOODS* (TGO 63) REMAIN RELEVANT TO THE REGULATION OF POLYMER URETHRAL CATHETERS FOR GENERAL MEDICAL USE, AND STERILE THERAPEUTIC DEVICES, RESPECTIVELY, ONLY UNTIL THE END OF THE TRANSITION PERIOD FOR THE NEW REGULATORY SYSTEM FOR MEDICAL DEVICES ON 4 OCTOBER 2007, THE THERAPEUTIC GOODS ADMINISTRATION DOES NOT PROPOSE TO AMEND EITHER ORDER.**

OTHER MATTERS

SECTION 5 – OTHER MATTERS

REPORT ON JOINT INTERIM EXPERT ADVISORY COMMITTEE ON STANDARDS

The Committee was given an update on work undertaken to date by the Joint Interim Expert Advisory Committee on Standards (JIEACS) and its Pharmacopoeial Standards Subcommittee. The fourth meeting of the Pharmacopoeial Standards Subcommittee, and the third meeting of JIEACS had been held in March 2007.

The Subcommittee considered the responses to the public consultation on microbiological standards for medicines and revised proposals on general requirements for tablets and capsules.

The JIEACS finalised its advice on the technical content of the draft Order on child-resistant packaging requirements for medicines, and also recommended a strategy for improving the performance of non-reclosable packaging as a child-barrier. The JIEACS also finalised its advice on the technical content of the draft Order on microbiological standards for medicines.

REPORT ON ANZTPA

The Committee was provided with an update on work towards the establishment of ANZTPA. It was noted that the supporting Bills for both Australia and NZ had been released – the NZ Therapeutic Products and Medicines Bill 2006 was proceeding through a government committee process following consultation, and the Australian Therapeutic Products Bill 2007 was undergoing stakeholder consultation.

It was noted that various technical rules and orders for ANZTPA were progressively undergoing stakeholder consultation and infrastructure issues to support the joint agency were being addressed.

CLOSE OF MEETING

The Committee noted that, in view of the commencement of ANZTPA, further Meetings of the TGC may not be necessary although the need for expert advice on standards matters could be unpredictable.

There being no further business for this meeting, the Chairperson closed the Meeting at 11.20 a.m.