Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

# Therapeutic Goods Committee

## *33RD MEETING (15-16 OCTOBER 2008)*

## *INFORMATION FOR STAKEHOLDERS – REPORT ON MEETING*

The 33rd meeting of the Therapeutic Goods Committee (TGC) was held in Conference Room 1, TGA Building, Narrabundah Lane, Symonston on 15 and 16 October 2008, between the hours of 1.30 pm and 5 pm on Wednesday 15 October 2008 and 9.15 am and 4 pm on Thursday 16 October 2008.

**Attendance:**

**Chairperson:** Associate Professor Loraine Holley

**Members:**
Mr David Clayton
Mr Michael Gepp
Dr Karen Hapgood
Dr Geoffrey Higgins
Mr Alan Leslie
Professor Klaus Schindhelm
Ms Anthea Steans
Ms Diane Walsh
Dr Meera Verma

**Apologies:** Ms Diane Walsh for part day on 16 October 2008

**TGA officers:**
Mr Mohammed Ali (part meeting)
Dr Peter Bird (part meeting)
Ms Vivienne Christ
Ms Trisha Garrett (part meeting)
Mr Philip K Harrison (part meeting)
Dr Larry Kelly (part meeting)
Ms Michelle McLaughlin (part meeting)
Dr Yook-Tau Pang (part meeting)
Ms Nicola Powell (part meeting)
Ms Sarah Todd (part meeting)

**Secretariat:**
Ms Margaret Joy
Ms Lyn Lewis (Secretary)

# AGENDA AND COMMITTEE ADMINISTRATION

## OPENING OF MEETING – WELCOME AND APOLOGIES

The Chairperson opened the Meeting at 1.30 pm, noting that this was the first Meeting of the Therapeutic Goods Committee (TGC) since the recent appointment of Members by the Parliamentary Secretary to the Minister for Health and Ageing.

Members were invited to introduce themselves and outline their particular area of interest/ expertise. Presentations were provided on the Therapeutic Goods Administration (TGA), the regulation of therapeutic goods in Australia including the role of the TGC in advising on matters relating to standards for therapeutic goods and the challenges of the anticipated regulatory reforms.

## TERMS OF REFERENCE AND MEMBERS' CONTACT DETAILS

Members noted the functions of the TGC as specified in regulation 34 of the Therapeutic Goods Regulations 1990 (the regulations) and that the Committee was of national importance with a role in ensuring, through its advice on standards, the quality and safety of therapeutic goods supplied in Australia.

Members were requested to check their contact details as currently held by the Secretariat and to advise of any errors or changes. Privacy considerations relating to the public release of Members' contact details were noted.

## ADOPTION OF AGENDA

The Committee adopted the agenda with a minor change to the sequence of considerations.

## CONFLICT OF INTEREST DECLARATIONS AND CONFIDENTIALITY REQUIREMENTS

The TGC discussed a range of issues relating to conflict of interest declarations and confidentiality requirements.

Members submitted their completed Disclosure of Interest Declarations in accordance with Committee procedures. Several potential interests were declared, and these were noted for consideration under the relevant agenda items.

## RATIFICATION PROCESSES AND MINUTES OF THE 32ND MEETING OF THE TGC

The TGC reviewed the processes previously adopted by the Committee for ratification, out-of-session, of Resolutions and Minutes of meetings, and the public release of key Resolutions and a report for stakeholders. These processes had been adopted by the TGC in 2001 in order to provide rapid advice to stakeholders of recommendations that may impact upon them, and also because public release of outcomes was consistent with the principles of transparency and accountability. The TGC agreed that the processes developed previously by the Committee should be continued.

The TGC then noted that the Resolutions and Minutes of the 32nd meeting of the TGC, held on 29 April 2008, had been ratified out-of-session in accordance with the processes outlined, and the key Resolutions from the meeting and a report for stakeholders were subsequently posted on the TGA internet site.

**RESOLUTION:**

**The Therapeutic Goods Committee (TGC):**

1. **AGREES that the processes developed by the TGC at its 19th Meeting, held in November 2001, for the ratification of Minutes out of session and the public release of key outcomes and a report on each meeting, should be continued.**

2. **NOTES that:**

   (a) **the Minutes of the 32nd Meeting of the TGC held on 29 April 2008 were ratified out-of-session as a true and accurate record of that Meeting; and**

   (b) **the documents *Summary of Key Resolutions* and *Information for Stakeholders – Report on Meeting* have been published on the TGA internet site.**

## STATUS REPORT OF ACTION ARISING FROM THE 32ND TGC MEETING

Members noted the report summarising the status of action arising from the 32nd TGC Meeting that had been held on 29 April 2008.

In relation to the making of Therapeutic Goods Order No. 80 *Child-Resistant Packaging Requirements for Medicines*, the Committee noted that further consideration would be given to the packaging of medicines containing glucosamine sulfate potassium chloride complex in 2009.

## SUBCOMMITTEE REPORTS

### Subcommittee on Biologicals

The TGC received a report on the establishment of the Subcommittee on Biologicals which had Terms of Reference "*To advise the TGC on standards for adoption in relation to the safety and quality of therapeutic goods that are human blood and blood components, blood products, human tissues, progenitor cells, cellular therapies and other products designated as biologicals*". All appointments to the Subcommittee had been made.

The first meeting of the Subcommittee was held on 23 July 2008 in Canberra, and the main consideration was the development of a draft standard for the minimisation of infectious disease transmission via human tissue based products, which would support the proposed new regulatory framework for human cells and tissue therapies and other emerging biological therapies (HCTs). The other item considered by the Subcommittee at that meeting was the need to update the existing standard in Australia for blood, blood components and plasma for fractionation.

The TGC noted the ratified report of the first meeting of the Subcommittee.

**RESOLUTION:**

**The Therapeutic Goods Committee:**

1. **NOTES that appointment of members to the Subcommittee on Biologicals was finalised in May 2008.**

2. **NOTES that the first meeting of the Subcommittee was held on 23 July 2008.**

3. **ACCEPTS the report of the first meeting of the Subcommittee, noting that further work is to be undertaken.**

## Subcommittee on Packaging Requirements for Therapeutic Goods

The TGC received a report on the establishment of the Subcommittee on Packaging Requirements for Therapeutic Goods, the role of which was to provide advice on matters relating to the packaging of therapeutic goods for human use. The Subcommittee's Terms of Reference identified three specific tasks:

- develop a best practice guideline on non-reclosable forms of packaging, such as blister or foil strip packaging, that will assist sponsors to improve the effectiveness of this style of packaging in reducing the potential for children to be accidentally poisoned by medicines packaged in this way;
- review the *Code of Practice for the Tamper-Evident Packaging (TEP) of Therapeutic Goods* (TEP Code of Practice) to determine whether it reflects current packaging technologies and stakeholder needs and update it as required; and
- review the relevance of Australian Standard AS 2216-1997, Packaging for Poisonous Substances, to therapeutic goods and develop a draft TGO for consultation with stakeholders that will effect the transfer of container requirements for therapeutic goods for human use from the Standard for the Uniform Scheduling of Drugs and Poisons to the TGA, as recommended by the National Competition Policy review of Drugs, Poisons and Controlled Substances Legislation and subsequently accepted by the Australian Health Ministers Advisory Council and Council of Australian Governments.

The TGC had recommended the composition of the subcommittee previously and the meeting now noted the membership.

The TGC noted that the first meeting of the Subcommittee would be held on Friday 7 November 2008.

**RESOLUTION:**

**The Therapeutic Goods Committee NOTES that the first meeting of the Subcommittee has been scheduled for November 2008.**

## SUMMARY AND STATUS OF THERAPEUTIC GOODS ORDERS

The TGC noted a report on the status of Therapeutic Goods Orders (TGOs) made under the *Therapeutic Goods Act 1989*. Since the April 2008 Meeting of the TGC, two new TGOs and one amendment to an existing TGO had been registered on the Federal Register of Legislative Instruments.

The new TGOs were:

- Therapeutic Goods Order No. 80 *Child-resistant packaging requirements for medicines* (Federal Register of Legislative Instruments (FRLI): Legislative Instrument - F2008L03428); and
- Therapeutic Goods Order No. 77 *Microbiological standards for medicines* (Federal Register of Legislative Instruments (FRLI): Legislative Instrument F2008L03574).

The Order that amended an existing TGO was Therapeutic Goods Order No. TGO 69B *Amendment to Therapeutic Goods Order No. 69 General requirements for labels for medicines* (Legislative Instrument - F2008L02056).

# MEDICINAL PRODUCTS

## DEVELOPMENT OF A THERAPEUTIC GOODS ORDER FOR ALL THERAPEUTIC GOODS CONTAINING HEPARIN

Prior to discussion of this item, Mr Leslie and Dr Verma declared potential conflicts of interest. In both cases, the potential conflict related to the Members' employers being sponsors of goods containing heparin. The determination was made that conflicts of interest did not exist and Mr Leslie and Dr Verma could take full part in the discussion.

The TGC was requested to advise on the proposal that a TGO be developed to specify the standard for therapeutic goods containing heparin. It was proposed by the TGA that the TGO require all therapeutic goods containing heparin to comply with the tests detailed in the monograph for heparin sodium published in the United States Pharmacopeia Revision Bulletin dated 18 June 2008 for the detection of the contaminant over-sulphated chondroitin sulphate (OSCS).

The Committee was provided with the background to this proposal, including information on the recall of a number of heparin products in 2008 following an observed increase in the USA of 'allergic/ anaphylactoid' type adverse events associated with the use of heparin for injection, the identification of the contaminant OSCS, and confirmation of the link between the presence and concentration of OSCS and the occurrence of adverse events.

Internationally, the United States Pharmacopeia (USP) and the European Pharmacopeia (Ph Eur) had updated their monographs for heparin to include tests to detect the contaminant OSCS and the TGA took the precaution of making it a condition of listing, registration or inclusion in the Australian Register of Therapeutic Goods for a range of therapeutic goods that contained heparin to comply with the updated USP monographs for heparin. However this condition could not be applied to therapeutic goods exempt from ARTG entry, which included many of the *in vitro* diagnostic devices (IVDs) that contained heparin.

The TGC was advised that the TGA was developing a strategy for ensuring the ongoing purity of heparin used in therapeutic goods supplied in Australia and, as part of this strategy, proposed that a TGO be developed to specify the standard for heparin used in therapeutic goods and in particular the need for heparin to be free from contamination with OSCS.

The TGC discussed the two test methods to detect OSCS that were included in the USP monographs for heparin. These were a Nuclear Magnetic Resonance (NMR) method, and a Capillary Electrophoresis (CE) method. While NMR was a highly sensitive test method, CE was a

broader test which could potentially detect other contaminants. It was proposed that OSCS should be 'not detectable' in samples tested according to either method and discussion followed on the meaning of not detectable and the difference between an impurity and a contaminant.

The TGC noted that further development of the TGO was being undertaken by the TGA, and that stakeholder consultation would be undertaken at the appropriate time.

**RESOLUTION:**

**The Therapeutic Goods Committee:**

1. **NOTES that the Therapeutic Goods Administration is developing a Therapeutic Goods Order that references the United States Pharmacopeia test for "over-sulphated chondroitin sulphate" as the standard for all therapeutic goods that contain heparin.**

2. **NOTES that it is proposed that the Therapeutic Goods Order have a 2 year sunset clause by which time it is expected that other mechanisms of control will be in place for these goods.**

## STATUS REPORT ON ADOPTION OF MULTIPLE PHARMACOPOEIAS AS DEFAULT STANDARDS

The TGC was provided with a status report on the adoption, under the *Therapeutic Goods Act 1989* (the Act), of the British Pharmacopoeia (BP), the European Pharmacopoeia (Ph Eur) and the United States Pharmacopeia-National Formulary (USP-NF) as equal default standards for medicines and other therapeutic goods that were not medical devices.

The TGC was informed that the necessary amendments to the Act were being prepared for consideration by the Australian Parliament. These amendments would allow sponsors to choose which default standard to apply to any particular product, unless one of the default standards dealt more specifically with the product concerned, or if there was a specific TGO in place. Sponsors would be required to observe all aspects of the chosen standard, rather than being permitted to choose the most favourable aspect of each. New editions of each of the default standards would be adopted automatically.

**RESOLUTION:**

**The Therapeutic Goods Committee NOTES that changes to the *Therapeutic Goods Act 1989* to adopt the British Pharmacopoeia, the European Pharmacopoeia and United States Pharmacopeia-National Formulary as equal default standards for medicines and other therapeutic goods that are not medical devices are being prepared for consideration by the Australian Parliament.**

## IMPLICATIONS OF MULTIPLE DEFAULT PHARMACOPOEIAS – RESOLUTION OF INCONSISTENCIES AND/OR CONFLICTS

The TGC was requested to consider the implications of amendments to the *Therapeutic Goods Act 1989* (the Act) to recognise the European Pharmacopoeia (Ph Eur) and United States Pharmacopoeia-National Formulary (USP-NF) in addition to the British Pharmacopoeia (BP) as equal default standards for medicines and other therapeutic goods that were not medical devices.

Specifically, the TGC was requested to consider the suitability of monographs of the USP-NF for biological products, blood products and water, and whether particular monographs of the USP-NF for such products were appropriate for adoption. The TGC was also requested to consider labelling implications arising from adoption of the USP-NF as a default standard.

*Biological products (including vaccines, antisera, antivenins, monoclonal antibodies and products of recombinant technology)*

Of the monographs for biological products included in the USP-NF, many contained no details of the specifications or test procedures with which the medicine should comply. Instead the monographs generally stated "conforms to the regulations of the FDA concerning biologics". In effect, the USP monographs for biological products acted as a signpost to the USA's Code of Federal Regulations (CFR) and the USA regulator, the Food and Drug Administration (FDA). The USP-NF therefore did not provide a monograph against which an Australian manufactured product could be readily evaluated in Australia or which was appropriate to apply under Australian law.

Specific concerns identified by the TGA from a comparison of monographs for biological products contained in the BP and the USP-NF had related to measurement of potency and the expression of this, and the lack of a test for thermal stability in monographs for live viral vaccines.

*Blood products*

The USP-NF also contained a number of monographs relating to products derived from fresh blood, fractionated plasma and tissues and, again, the monographs referred to other documents (e.g. CFRs, FDA guidances) and did not stand alone.

Specific differences between the BP/Ph Eur and the USP-NF monographs of concern to the TGA related to the USP-NF not specifying a potency test method, the absence of a requirement in the USP-NF for mandatory Nucleic Acid Amplification Testing (NAT) of starting plasma, and the level of product characterisation being deficient in the USP-NF compared to the Ph Eur.

*Water*

The TGC was advised that the TGA held concerns over the USP-NF monographs for water used for the preparation of medicines for parenteral injection. Specifically, non-sterile Water for Injection USP was of unspecified microbiological quality and the TGA was concerned that it could contain sufficient bioburden to increase failures when a product was sterilised by filtration. In addition, Water for Injection USP was allowed to be manufactured by "distillation or a purification process that is equivalent or superior to distillation in the removal of chemicals and microorganisms", which the FDA took to include reverse osmosis systems. However the TGA held the view that there was insufficient evidence to demonstrate that reverse osmosis systems could consistently produce water of a quality at least equal to that produced by distillation. Also, the BP/Ph Eur specified a limit for microbial contamination for Purified Water BP whereas the USP-NF did not have a microbial contamination limit for Purified Water USP.

*Other concerns*

Several other aspects of USP-NF monographs that were of potential concern were noted. These included assays that were measured against a standardised USP Reference Standard and were expressed in USP Units which differed from International or metric units, and the wider limits allowed for the content of the active ingredient in antibiotic products than permitted by the BP.

Potential issues with the labelling of medicines if the requirements of the USP-NF were implemented in full were noted, in particular if an active ingredient was assayed in USP units and these units were used on the label rather than International or metric units. Amendment to Therapeutic Goods Order No. 69 *General requirements for labels for medicines* (TGO 69) may be necessary to resolve labelling issues.

*Discussion*

The TGC recognised that individual monographs of the BP (or Ph Eur) and the USP-NF for the same therapeutic good may specify different and sometimes inconsistent requirements, and discussed the proposal put forward by the TGA that the applicable standards for biological products and blood products should be those of the BP or Ph Eur in cases where the USP-NF referenced other USA documents or requirements. This could be achieved through the development of new TGOs.

It was noted that the TGA also proposed that the applicable standards for water should be those of the BP or Ph Eur and that this too could be achieved through a new TGO.

In practice, the effect of such TGOs would be to maintain the *status quo* for existing products (which currently were required to comply with the BP) and prevent new products using the USP-NF as their default standard. This would be particularly relevant to products manufactured in the USA.

The TGC agreed that it would be appropriate for stakeholder consultation to be undertaken on the series of proposals put forward by the TGA and it was likely that this consultation would draw out further comments on the impact. In relation to labelling, the Committee noted that TGO 69 currently only specified the use of International Units on labels for certain types of products and therefore TGO 69 should be amended.

**RESOLUTION:**

**The Therapeutic Goods Committee:**

**1. NOTES:**

**(a) that changes to the *Therapeutic Goods Act 1989* (the Act) to adopt the British Pharmacopoeia, the European Pharmacopoeia and United States Pharmacopeia-National Formulary (USP-NF) as equal default standards for medicines and other therapeutic goods that are not medical devices will inevitably lead to the situation of individual monographs for the same therapeutic good specifying different and sometimes inconsistent requirements; and**

**(b) that in a small number of cases such differences could have clinical consequences or create regulatory problems.**

**2. NOTES that the Therapeutic Goods Administration has identified the following situations as being of concern:**

**(a) where monographs of the USP-NF for biological products are not 'stand alone' but reference or rely upon United States (US) legislation and decisions of the US Food and Drug Administration (FDA);**

**(b) where monographs of the USP-NF for blood products are not 'stand alone' but reference or rely upon US legislation and decisions of the US FDA;**

**(c) where USP Units used in assays and potency testing conducted in accordance with the USP-NF are not interchangeable with International Units or metric units, with potential for product labelling in USP Units to be confusing to users; and**

**(d) where monographs of the USP-NF for water for injection permit production of water by methods other than distillation, leading to concerns about microbiological quality.**

**3. PROPOSES that a new Therapeutic Goods Order be developed to specify that biological products should comply with the British Pharmacopoeia or the European Pharmacopoeia, and not the USP-NF, in cases where the USP-NF references other US documents and requirements.**

**4. PROPOSES that a new Therapeutic Goods Order be developed to specify that blood products should comply with the British Pharmacopoeia or the European Pharmacopoeia, and not the USP-NF, in cases where the USP-NF references other US documents and requirements.**

**5. PROPOSES that amendment to Therapeutic Goods Order No. 69 *General Requirements for Labels for Medicines* be made to require the expression on labels of quantities to be in metric or International Units, and to disallow labelling in USP Units.**

**6. PROPOSES that a new Therapeutic Goods Order be developed to specify that water for injection should comply with the British Pharmacopoeia or the European Pharmacopoeia, and not the USP-NF.**

**7. RECOMMENDS that these new or amended Therapeutic Goods Orders should be released for stakeholder consultation.**

**8. AGREES to consider stakeholder responses on the draft Therapeutic Goods Orders with the aim of finalising the new Orders, if agreed, to suit the timetable for the introduction in the Act of the European Pharmacopoeia and the USP-NF as equal default standards to the British Pharmacopoeia.**

## BRITISH PHARMACOPOEIA 2009

The TGC was requested to advise on whether, notwithstanding the planned recognition of multiple default pharmacopoeias under the *Therapeutic Goods Act 1989* (the Act), stakeholders should be consulted on the adoption of British Pharmacopoeia 2009 (BP 2009) as the edition of the British Pharmacopoeia (BP) defined under existing legislation. This would be a precautionary measure, to guard against a superseded edition of the BP remaining the default standard for an extended time if there was a delay in the passage by Parliament of the planned amendments to the Act.

The TGC noted that, until such time as the Act was amended to recognise multiple default pharmacopoeias, the BP would remain the only default standard in Australia for medicines and other therapeutic goods that were not medical devices. Unless an Order was made to amend the

definition contained in the Act for the BP, BP 2008 would remain in force despite BP 2009 being published and entering into force in the United Kingdom.

As the timing for passage through Parliament of the planned amendments to the Act was not certain, the TGC considered it would be prudent to prepare for an update to the definition of BP contained in the existing Act.

**RESOLUTION:**

**The Therapeutic Goods Committee (TGC):**

1. **NOTES that the British Pharmacopoeia 2009 (BP 2009) has been published and will enter into force in the United Kingdom (UK) on 1 January 2009.**

2. **NOTES that notwithstanding the planned recognition of multiple pharmacopoeias 'as amended from time to time' as equal standards under the *Therapeutic Goods Act 1989* (the Act), the timing for this legislative change is at the discretion of the Parliament.**

3. **CONSIDERS that it would be prudent to consult with stakeholders on the adoption of BP 2009 as the default standard under existing therapeutic goods legislation as an interim measure to avoid a superseded edition of the British Pharmacopoeia remaining the default standard for an extended time.**

4. **REQUESTS that the Therapeutic Goods Administration undertake this stakeholder consultation on behalf of the TGC.**

5. **AGREES to consider the outcomes of the consultation at its next Meeting, at which time the need for amendment to the edition of the British Pharmacopoeia currently specified in the Act should be clearer.**

## STANDARDS FOR ANTHROPOSOPHIC AND HOMOEOPATHIC MEDICINES

Mr Gepp declared a potential conflict of interest, in that he was employed in the complementary medicine industry. The determination was made that a conflict of interest did not exist and Mr Gepp could take full part in the discussion.

The TGC was informed of the TGA consultation paper *Regulation of Homoeopathic and Anthroposophic Medicines in Australia*, and the proposed changes to the *Therapeutic Goods Act 1989* (the Act) relating to standards for homoeopathic and anthroposophic medicines that were described in the consultation paper.

Information was provided on the background to the proposed regulatory reforms and the possible changes to the way homoeopathic and anthroposophic medicines were regulated in Australia. The Committee was advised that implementation of the reforms would involve amendment to a range of legislative documents and the changes of relevance to the TGC were the proposed amendment of section 10 of the Act to include a range of specialist pharmacopoeias as the standards for homoeopathic and anthroposophic medicines, and some changes to labelling requirements.

The list of proposed pharmacopoeias for anthroposophic medicines and homoeopathic medicines that had had been included in the consultation paper was noted. The TGA considered that such a

range of pharmacopoeias was necessary in order to allow the supply in Australia of products originating from different countries and because homoeopathic pharmacopoeias had evolved differently over time in different countries.

A late paper presented to the Committee indicated that, in response to the consultation, stakeholders had made few comments about the proposed pharmacopoeial standards for homoeopathic and anthroposophic medicines. Addition of the *Pharmacopoeia Helvetica* had been proposed on the basis that this pharmacopoeia contained valuable references for anthroposophic medicines, although the TGA had not yet reached a position on this suggestion. Also mentioned in the responses was the *Homoeopathic Pharmacopoeia of India* and comments were made concerning the *British Homoeopathic Pharmacopoeia*, which was no longer current.

In relation to other matters discussed in the consultation paper, the TGC was advised that consideration of good manufacturing practice requirements was ongoing, and that labelling matters specific to homoeopathic and anthroposophic medicines should be addressed as part of TGC's ongoing consideration of requirements for the labelling of medicines.

**RESOLUTION:**

**The Therapeutic Goods Committee (TGC):**

1. **NOTES the Therapeutic Goods Administration's consultation paper *Regulation of Homoeopathic and Anthroposophic Medicines in Australia* which was released for stakeholder comment in August 2008.**

2. **NOTES the proposal contained in the consultation document that the *Therapeutic Goods Act 1989* (the Act) be amended to include a range of alternative default standards for homoeopathic medicines and anthroposophic medicines.**

3. **ENDORSES, in principle, that the Act should allow for appropriate and specific default standards for homoeopathic and anthroposophic medicines.**

## MEDICINE LABELLING – STAKEHOLDER CONSULTATION ON DRAFT THERAPEUTIC GOODS ORDER NO. 79 *GENERAL REQUIREMENTS FOR THE LABELLING OF MEDICINES*

The TGC was requested to review the draft new Therapeutic Goods Order (TGO) on medicine labelling, Draft Therapeutic Goods Order No. 79 *General Requirements for the Labelling of Medicines* (TGO 79 draft), which had undergone stakeholder consultation in early 2008, and develop a strategy to progress the proposed changes to labelling requirements for medicines. Consideration of this item had been deferred by the TGC at its last meeting as the consultation had identified some complex issues and differences of opinion among stakeholders that would not be resolved easily.

The TGC noted current labelling requirements for medicines given in Therapeutic Goods Order No. 69 *General requirements for labels for medicines* (TGO 69) and the history of review of these by the TGC and the Joint Expert Committee on Trans Tasman Labelling Requirements for Medicines (JECLM) over the past five years. TGO 79 (draft) had been based on the draft labelling Order developed by JECLM for application under the proposed, but now postponed, joint Australia and New Zealand regulatory scheme for therapeutic goods.

The consultation had elicited 59 submissions and, although some comments were of a general nature, many related to specific proposals given in the draft TGO.

The main comments from the industry sector related to the proposed transition timeframe, the impact of the proposed changes across medicines, the practicality of some of the proposed requirements particularly for small containers, and the continuation of multiple documents relating to labelling requirements.

Consumer organisations supported the intention to expand the list of excipients that required label declaration, on the basis of consistency with food labelling requirements and improving safety for those who may be allergic to particular ingredients, and contribution of the label to the quality use of medicines.

Comments from the professional areas and government agencies focused on the role of medicine labels in achieving quality use of medicines, and recommended further changes to reduce potential for dispensing and administration errors, give greater emphasis to generic medicine names rather than trade names, and address issues of label legibility and presentation that were considered problematic.

The TGC noted that the stakeholder responses had indicated that the impact on industry of implementing TGO 79 as drafted would be considerable, and it may not deliver the desired benefits for consumers and health professionals. Therefore options to progress the revision of labelling requirements for medicines would include either proceeding with adoption of an amended version of TGO 79 or recommending specific amendments to TGO 69 to implement those changes which were considered to be important in the short-term, for example those that were safety related. The potential impact on industry of multiple, sequential, changes to labelling requirements occurring over a short period of time was noted.

The Committee discussed the adequacy of TGO 69 and whether its requirements were causing any safety concerns. TGO 69 was considered to be reasonably satisfactory and, subject to amendment to resolve any safety issues, could remain in force. However a number of changes in the external environment, for example the promotion of generic medicines, would need to be taken into account.

One key issue for consideration would be the presentation of active ingredient names on the labels of prescription medicines, and this was discussed further. It was questioned whether the proposed increase in letter height from 1.5 mm to 2 mm would improve safety and increase consumer awareness. Stakeholders had either sought no change from current requirements or alternatively a greater increase than had been proposed. Equal prominence of both names was recommended in the *Best Practice Guideline on Prescription Medicine Labelling*, but it was suggested that the real issue was not about font size *per se* but the need for consumers to know and be able to recognise the generic names of their medicines. This was the focus of an education campaign currently being conducted by the National Prescribing Service.

The TGC noted that a number of expert bodies considered that a larger font size would improve safety, but this was a complex and multifactorial issue. For example, pharmacists had a responsibility to ensure the patient was aware of the generic names of medicines dispensed for them, and occasions of patients not recognising the generic names of medicines and consequently double-dosing with two different brands were exacerbated by differences in the appearance of tablets/capsules, multi-drug therapy and the patient not knowing what condition each medicine was intended to treat. As different groups had different views on the issue and conflicting demands, it

was likely that compromises on both sides would be needed. The TGC agreed that the prominence of active ingredient names was a significant issue for progression.

The TGC then reviewed a summary of the main differences between current labelling requirements, as given in TGO 69, and the proposed new labelling requirements, as given in TGO 79 (draft). The following table summarises the Committee's views and gives priorities for action.

| Difference from TGO 69 | TGC comment |
|---|---|
| Inclusion of new definitions | Whether new definitions were necessary would depend on the extent of amendment of TGO 69 and whether the new concepts described in the definitions were progressed. Definitions would be introduced as required. |
| Label presentation – changes to font size requirements | Font size requirements for active ingredient names in prescription medicines as discussed above - for further review.<br>Proceed with proposed reduction to 1 mm for all information except SPF on sunscreen preparations in containers with capacity of not more than 25mL or 25 g – this had not drawn stakeholder comment. |
| Label presentation - requirement for colour contrast and durability of the label itself | These proposed requirements were considered to reflect good practice, but to a large extent were covered by existing requirements of TGO 69 (visibility, durability and legibility). However problems with the legibility of embossing/debossing had been raised in a number of stakeholder submissions and, together with the issue of colour contrast, should be further considered. |
| Particulars to be on the label – excipient declarations for prescription medicines to appear on the label of the medicine or in a leaflet packaged with the medicine, rather in the Consumer Medicine Information (CMI), MIMS Annual or the Australian Prescription Products Guide | Industry stakeholders had strongly opposed this on the basis that it would force reversion from the electronic delivery of CMI to enclosure of hard copy in the packaging, and the consequence of this would be that the ability to rapidly amend CMI to update safety information would be lost.<br>Requirements of the labelling Order should not to be an impediment to the effective delivery of up-to-date CMI to consumers. It would be preferable for the provision of CMI to be improved, and support should be given to initiatives to advance this. Better availability of CMI to consumers would ensure excipient information for prescription medicines was readily available.<br>The TGC requested that the TGA convey to the Department of Health and Ageing the Committee's support of arrangements that foster CMI provision by pharmacists. |
| Particulars to be on the label – excipient declarations to appear on both the container and primary pack labels rather than primary pack alone | This would be beneficial, but was considered to be a change of lower priority than others. |

| Difference from TGO 69 | TGC comment |
|---|---|
| Particulars to be on the label – the label on all injections and any other ampoules must state the route of administration | This was considered to be a safety issue and therefore should be progressed. The proposal had not drawn stakeholder comment. |
| Particulars to be on the label - condition for shift of active ingredient names to side or rear panel changed from 4 or more active ingredients to 5 or more active ingredients for registered medicines; and shift of active ingredient names in herbals, vitamins and/or mineral products to side or rear panel extended to all listed medicines with two or more active ingredients | These were considered to be changes of low priority. |
| Particulars to be on the label - quantity of the goods to be stated on injections | This should be considered in conjunction with further review of the expression of statement strength on injections. |
| Particulars to be on the label – a primary pack enclosing more than one container of the same medicine to include a statement of the number of containers within the primary pack. | This would be beneficial, but was considered to be a change of lower priority than others. |
| Specification of minimal requirements for labelling opaque intermediate packaging if used. | While desirable that intermediate packaging included the information listed in TGO 79 (draft), this proposal had been based on a practice issue (separation of inner packs from the primary pack). The types of products involved were generally low volume products, which may be packaged overseas. Implementation may therefore be difficult. As an alternative to inclusion in TGO 69, the proposed requirements could be considered for inclusion in the *Best Practice Guideline on Prescription Medicine Labelling*. |
| Qualifications and Special Requirements – inclusion of a new section specifying label requirements for the outer container of a medicine kit | This would be beneficial, and had not been contentious in the stakeholder consultation. Although considered to be a change of lower priority than others, it could potentially be added in the future. |
| Qualifications and Special Requirements – inclusion of a new section specifying space for addition of patient details and other dispensing information on starter packs | This would be beneficial, but was considered to be a change of lower priority than others as it duplicated, to a large extent, requirements of the Medicines Australia Code of Conduct. |
| Qualifications and Special Requirements – revised requirements for small containers and equivalent size injections, and introduction of new provisions relating to very small containers (no more than 2 mL) and equivalent size injections | Resolution of difficulties with the labelling of small containers should be progressed, but the proposed requirements warranted further review as stakeholder comments indicated that issues remained around the amount of information to be included on the labels. Stakeholders also raised issues with the proposed delineation of container sizes at 2 mL and 20 mL. |
| Qualifications and Special Requirements – homoeopathic medicines and formulations containing both homoeopathic preparations and non-homoeopathic ingredients | Proposed requirements would need to be refined after consideration of stakeholder comments on the proposed new regulatory framework for homoeopathic and anthroposophic medicines. |

| Difference from TGO 69 | TGC comment |
|---|---|
| Qualifications and Special Requirements – revised concessions for strip, blister and dial dispenser packs (including distinction between calendar and compliance packs), and individually wrapped goods | Stakeholders had raised several issues that warranted consideration. Proposals to be reviewed and further considered. |
| Qualifications and Special Requirements – plastic ampoules - clarification of wording and intent, for ampoules with nominal volume less than 5 mL attached to a connecting strip – same requirements whether or not the seal is broken on detaching an ampoule and inclusion of batch numbers and expiry dates on individual ampoules not the connecting strip. | Some issues common to all small and very small volume injections were raised by stakeholders. Whether the inclusion of batch and expiry details on plastic ampoules would be difficult from a manufacturing perspective needed further consideration. |
| Use of appropriate metric units – addition of several statements clarifying requirements | This would be beneficial, but was considered to be a change of low priority. |
| Expression of quantity or proportion of active ingredients – several proposed changes including for transdermal patches (strength to be as total quantity in each patch in addition to release rate), all injections larger than 1 mL (include total quantity in total volume in addition to quantity per mL), and use of retinol equivalents for vitamin A content | Significant issues had been raised by stakeholders, and expression of content/strength was a safety issue. The expression of quantity or proportion of active ingredients in liquids for oral administration had also been raised by a stakeholder as a safety issue. These matters all required further consideration.<br>The labelling of vitamin A content was addressed under another agenda item and it was suggested that the expression of content where the active ingredient was an herbal extract also should be reviewed. |
| Permitted statements of storage conditions – inclusion of some additional statements | The proposed new statements built on statements that were already permitted. TGO 69 did not prevent the inclusion of additional information on labels; therefore the proposed new statements would already be permissible. Amendment of the Order to specify the statements therefore was low priority. |
| Excipients to be declared on labels [First Schedule] – inclusion of some additional excipients to the First Schedule (crustacean & crustacean products, egg & egg products, fish & fish products, milk & milk products, potassium salts, sesame seed & sesame seed products, soya beans & soya bean products, and tree nuts & tree nut products); and other amendments including inclusion of new requirements for statements regarding potential for severe allergic reaction to pollen, propolis and royal jelly. | These proposals were clearly safety related and should be progressed following resolution of matters raised by stakeholders. |

The TGC noted that no proposal had been included in TGO 79 (draft) for there to be a mandatory requirement for the label of prescription medicines to have a clear space for attachment of a dispensing label. However the need for this had been stressed by many of the health professionals

responding to the consultation. The TGC agreed to give further consideration to this suggestion also.

**RESOLUTION:**

**The Therapeutic Goods Committee:**

**1. NOTES:**

**(a) the draft Therapeutic Goods Order on medicine labelling [Therapeutic Goods Order No. 79 *General Requirements for the Labelling of Medicines* (TGO 79) (draft)] which underwent stakeholder consultation in January-February 2008; and**

**(b) the large number of stakeholder responses to TGO 79 (draft), which were varied and raised significant matters for consideration.**

**2. IDENTIFIES the matters listed below for further review:**

**(a) batch and expiry dating of individual plastic ampoules that are joined to a connecting strip;**

**(b) expansion of the First Schedule to include additional excipients that must be declared on labels;**

**(c) expression of quantity or proportion of active ingredient in transdermal patches;**

**(d) expression of quantity or proportion where an active ingredient is a herbal extract;**

**(e) inclusion of the route of administration on all injections and on any other medicine contained in an ampoule, whether or not for injection;**

**(f) legibility requirements including issues of colour contrast and embossing/debossing;**

**(g) prominence of active ingredient names (font size and position);**

**(h) requirements and concessions for small and very small containers and equivalent sized injections (required information and definitions);**

**(i) requirements and concessions for strip, blister and dial dispenser packs and individually wrapped goods;**

**(j) requirements for homoeopathic and anthroposophic medicines to apply under the proposed new framework for the regulation of homoeopathic and anthroposophic medicines in Australia;**

**(k) space allowance on prescription medicines for placement of a dispensing label; and**

**(l) statement of volume on injections and expression of strength on liquids for oral administration and injections.**

**3. RECOMMENDS that, rather than implementing TGO 79 at this time, the initiatives identified above should be progressed as possible amendments to Therapeutic Goods Order No. 69 *General Requirements for Labels for Medicines* (TGO 69).**

**4. NOTES that independently to the consultation on TGO 79 (draft), the following additional matters relating to medicine labelling have been identified as warranting consideration for inclusion in TGO 69 as mandatory requirements:**

**(a) bar coding of medicines or particular types of medicines; and**

**(b) inclusion of identifying information on transdermal patches.**

## UPDATE TO EDITION OF *REQUIRED ADVISORY STATEMENTS FOR MEDICINE LABELS* (RASML) REFERENCED IN THERAPEUTIC GOODS ORDER NO. 69 *GENERAL REQUIREMENTS FOR LABELS FOR MEDICINES*

The TGC was asked to advise on a proposal to amend Therapeutic Goods Order No. 69 *General requirements for labels for medicines* (TGO 69) to adopt the September 2008 version of the document *Required Advisory Statements for Medicine Labels* (RASML), and to change the expression of vitamin A content from International Units to retinol equivalents, so that the units of measurement used in the statement of content would be consistent with those in associated warning statements.

The TGC noted the background to the inclusion of reference to RASML in TGO 69, and that RASML was the key document giving the warning statements that must be included on the labels of medicines. TGO 69 needed to specify a particular version of RASML however, as it was not possible legislatively to refer to that document 'as amended from time to time'.

Currently TGO 69 referred to the April 2006 version, although there had since been two further updates (April 2008 and September 2008). The RASML document currently published on the TGA's website was the September 2008 version and unless that version was referred to in TGO 69, any new or amended requirements included in that update, as well as those in the April 2008 version, were not supported by appropriate legislation. The TGC was advised that stakeholder consultation, undertaken in accordance with the process outlined in the RASML document, had occurred on the proposed April 2008 and September 2008 amendments prior to their finalisation.

In relation to vitamin A, the TGC noted that the RASML included a requirement for medicines containing Vitamin A, above specified cut-off limits, to carry warning statements regarding recommended daily amounts, and that amounts in excess of another specified amount can cause birth defects. The April 2008 version of RASML amended the entry for vitamin A to describe the cut-off limits and advice on doses above which birth defects can occur in terms of retinol equivalents rather than International Units. This change to RASML resulted from the need to align with the terminology used in the Standard for the Uniform Scheduling of Drugs and Poisons for cut-offs for poisons scheduling, which itself had been amended to align with the expression of

Nutrient Reference Values for vitamin A determined by the National Health and Medical Research Council.

Without a consequential amendment to TGO 69, which specified that the vitamin A content of medicines must be quantified on the label in International Units, there would be potential for mismatch between declaration of vitamin A content and the limits specified in the warning statements. This would be confusing for consumers, and have potential to result in incorrect dosing.

The TGC advised that amendment of the definition of RASML contained in TGO 69 was appropriate and that a corresponding amendment should be made to require the content of vitamin A content to be expressed in retinol equivalents.

Members considered that there may be some issues with transition arrangements and the timing of the changes. The transition period built into RASML allowed a 12 month period from date of gazettal (23 April 2008) for warning statements on existing products to be amended and, to ensure consistency, the amendment to TGO 69 to require the use of retinol equivalents in the statement of content would need to have the same effective date. However, some sponsors may already have made the change to their warning statements on vitamin A products or intend to implement it prior to the end date given by RASML for the transition, notwithstanding the fact that TGO 69 had not yet adopted a version of RASML that required the use of retinol equivalents instead of International Units.

The Committee noted that the option of a sponsor seeking an exemption from compliance with a standard or a particular aspect of a standard under s14/14A of the Act may be a relevant mechanism to address such issues, and requested that the TGA ensure that administrative processes were in place to resolve anomalies between the expression of vitamin A content on the label of medicines and required vitamin A warning statements until such time as the recommended amendments to TGO 69 became effective.

**RESOLUTION:**

**1. The Therapeutic Goods Committee:**

**(a) NOTES that the definition of *Required Advisory Statements for Medicine Labels* (RASML) contained in Therapeutic Goods Order No. 69 *General Requirements for Labels for Medicines* (TGO 69) refers to the version of RASML dated April 2006;**

**(b) NOTES that the current version of RASML, as published on the Therapeutic Goods Administration (TGA) internet site, is dated September 2008;**

**(c) NOTES that the April 2008 and September 2008 updates to RASML followed stakeholder consultation undertaken by the TGA, and all updates have been gazetted; and**

**(d) RECOMMENDS that the definition of *Required Advisory Statements for Medicine Labels* contained in clause 2, Interpretation, of TGO 69 should be amended to refer to the September 2008 version of that document.**

**2. The Therapeutic Goods Committee:**

**(a) NOTES that warning statements for medicines containing Vitamin A that are included in the current version of RASML express Vitamin A content in retinol equivalents;**

**(b) RECOMMENDS that a consequential amendment be made to TGO 69 to require the statement of quantity or proportion of Vitamin A contained in medicines also to be expressed in retinol equivalents; and**

**(c) REQUESTS that the TGA ensure that administrative processes are in place to resolve anomalies between the expression of Vitamin A content on the label of medicines and any required Vitamin A warning statements until such time as the recommended amendments to TGO 69 become effective.**

## LABELLING OF TRANSDERMAL PATCHES

The TGC was requested to consider a recommendation made by the Medicines Evaluation Committee that all transdermal patches should include, on the patch itself, sufficient information to allow identification of the patch.

The TGC was advised of concerns that patients using patches sometimes entered hospital in a confused or unconscious state or were anaesthetised for surgery and the medical staff was unable to identify their patches and thus determine the appropriate medication for such patients. Cases also had been reported of serious adverse events or reduced therapeutic efficacy resulting from interactions between drugs administered and those in patches that patients were wearing. These problems were compounded by the lack of a consolidated list of patches, with descriptions, that would assist in their identification.

The Medicines Evaluation Committee (MEC) had discussed this issue and had recommended that all transdermal patches, whether registered or listed, should be clearly labelled with the drug name and the strength. The MEC also recommended that the TGC be asked to consider the matter and determine an appropriate standardised method of labelling patches.

The Committee was advised now that there were approximately 100 transdermal patches registered or listed in Australia – approximately 60 prescription products, about 35 non-prescription products and about 8 patches delivering various complementary medicines consisting of mixtures of herbal extracts. Generally, these patches were packaged in sachets that were adequately labelled and clearly identified the patch enclosed. However, there were no specific requirements for labelling of the actual patches and in practice this varied from patches showing a brand name and/or the drug name and strength, to the use of an identifying code of letters and/or numbers, and in worst cases having identifying marks at all.

The TGC discussed general issues surrounding the labelling of transdermal patches, including privacy considerations for patients wearing patches and the balance of this against safety considerations. It also was noted that many transdermal patches were manufactured overseas, and hence the consideration of whether a labelling requirement for transdermal patches was feasible needed to take that into account.

The TGC accepted that consideration needed to be given to the MEC recommendation, but clearly more information on the presentation of existing transdermal patches and the potential for inclusion of defined identifying information was necessary. To inform its consideration, the TGC requested

that, as an initial step, comment be sought from the relevant product regulators. The TGC would then consider this matter as part of its further review of TGO 69.

**RESOLUTION:**

**The Therapeutic Goods Committee (TGC):**

1. **NOTES the recommendation made by the Medicines Evaluation Committee that all transdermal patches should be labelled with sufficient information to allow identification of the patch, including the active ingredient and the strength, after application to a patient.**

2. **RECOMMENDS that:**

   (a) **the labelling of transdermal patches and the need for inclusion of identifying information on the patch itself be considered as part of the TGC's further review of Therapeutic Goods Order No. 69 *General Requirements for Labels for Medicines*; and**

   (b) **to inform that consideration, comment be sought from the relevant product regulators on the presentation of existing transdermal patches and the potential for inclusion of identifying information when not already shown.**

## INCLUSION OF BAR CODES ON MEDICINE LABELS

The TGC was requested to give preliminary consideration to a proposal for the mandatory bar coding of medicines, based on the potential of bar coding to improve patient safety through reducing dispensing errors.

The TGC noted that a number of responses to the stakeholder consultation on draft Therapeutic Goods Order No. 79 *General Requirements for the Labelling of Medicines* (TGO 79 draft) stressed the need for bar coding to become a mandatory label requirement, particularly for prescription medicines:

- The Australian Commission on Safety and Quality in Healthcare had stated that the use of barcode technology within the dispensing and drug administration process was an important strategy for reducing medication errors but one of the barriers to implementing barcode checking within the medication management pathway was non-uniform inclusion of barcodes on pharmaceutical packaging.
- Other stakeholders (the Pharmaceutical Benefits Division and the Society of Hospital Pharmacists of Australia) supported the inclusion of barcodes on medicine labels, although one stakeholder recommended that the requirement be expressed in terms of "Machine Readable Coding" in order to permit the use of other technologies such as microdots and Reduced Space Symbology.

Recent correspondence from the Pharmacy Board of Victoria provided information on the contribution of lack of barcodes to dispensing errors, and also on the status of jurisdictional requirements for pharmacies to be equipped with scanners. The Pharmacy Board of Victoria estimated that up to 10 per cent of prescription products did not have a barcode and raised a number of issues around mandatory bar coding of medicines for consideration (control over issue of bar codes, format and positioning of the bar code, and challenges of small volume containers).

The TGC advised that bar coding requirements for medicines needed to be considered in the global context and recommended that further information be sought on bar code technologies and formats, current industry practice in Australia and overseas, and international regulatory practice.

One issue was what information a bar code should contain, as bar codes that included batch and expiry details (e.g. EAN 128 codes) would need to be applied on the packaging line rather than pre-printed, with cost and process implications. Related to this was the question of whether pharmacy scanners did or could record batch details, which was not thought to be the case. Neither at this time did wholesalers record batch details of medicines they distributed. Other technologies such as Radio Frequency Identification (RFID) tags and microdots, which may offer similar benefits to bar coding, needed further investigation as specifying bar coding, may tie manufacturers to technology that would soon be superseded.

It also was noted that, while there may already be trend for prescription medicines to include bar codes, fewer complementary medicines did, and checking against a prescription generally was not relevant. Therefore the consideration of mandatory bar coding may need to be sector specific.

The TGC agreed that consideration of introducing mandatory requirements for bar coding should be given high priority but further information on current Australian and international practice, as well as international regulatory requirements would be needed to inform the consideration.

**RESOLUTION:**

**The Therapeutic Goods Committee:**

1. **NOTES that the inclusion of bar codes on medicines has potential to improve patient safety through reducing dispensing errors.**

2. **NOTES the increasing use of bar code scanners in pharmacies as a routine part of the dispensing process.**

3. **AGREES that consideration of mandatory bar coding requirements for medicines should be given high priority.**

4. **REQUESTS that the Therapeutic Goods Administration gather further information on bar code technologies and formats, current industry practice in Australia and overseas, and international regulatory practice, for consideration by the Therapeutic Goods Committee.**

## STANDARDS FOR EXPORT ONLY MEDICINE

Prior to discussion of this item, Mr Gepp declared a potential conflict of interest, as his employer was a sponsor of export only medicines. The determination was made that a conflict of interest did not exist and Mr Gepp could take full part in the discussion.

The TGC was requested to advise on whether the editions of the British Pharmacopoeia (BP), United States Pharmacopeia-National Formulary (USP-NF), Japanese Pharmacopoeia (JP) and European Pharmacopoeia (Ph Eur) referenced in Therapeutic Goods Order No. 70B *Standards for Export Only Medicine* (TGO 70B) should be updated to refect the current editions.

The TGC recalled the rationale to the development of Therapeutic Goods Order No. 70 *Standards for Export Only Medicine* (TGO 70), which commenced operation in May 2002 and permitted export only medicines to meet specific standards other than those currently applied under subsection 10(2) of the *Therapeutic Goods Act 1989* (the Act). The Order made USP-NF, Ph Eur and JP, in addition to BP, acceptable standards for medicines which were for export only. However publication of new editions of the pharmacopoeias referenced in the Order meant that it routinely needed to be updated to maintain its currency. This had occurred twice previously, through TGOs 70A and 70B, and it was noted that the pharmacopoeias referenced in the Order had again been superseded by new editions.

The TGC supported the update of TGO 70B to reflect the current editions of the referenced pharmacopoeias and noted that the TGA was consulting with Medicines Australia, Australian Self Medication Industry Inc. and the Complementary Healthcare Council on the proposal.

Following this discussion, the TGC was provided with a summary of the proposed new arrangements for the export of medicines that were included in the TGA's regulatory reform package. It was noted that the proposed new arrangements were intended to provide Australian medicine exporters with more flexibility, without compromising the quality and safety of export medicines. The matter of appropriate standards for export only medicines was addressed in a draft consultation paper, and the TGC noted that further consideration of standards for export only medicine would be likely following conclusion of the consultation.

**RESOLUTION:**

1. **The Therapeutic Goods Committee RECOMMENDS that Therapeutic Goods Order No. 70B *Standards for Export Only Medicine* be amended to update the references to all pharmacopoeias included in it, as follows:**

   **(a) British Pharmacopoeia 2005 be amended to British Pharmacopoeia, with the edition to be that defined under the *Therapeutic Goods Act 1989*;**

   **(b) European Pharmacopoeia 5th edition be amended to European Pharmacopoeia 6th edition;**

   **(c) United States Pharmacopeia 29th edition-National Formulary 24th edition be amended to United States Pharmacopeia 31st edition-National Formulary 26th edition; and**

   **(d) Japanese Pharmacopoeia 14th edition be amended to Japanese Pharmacopoeia 15th edition.**

2. **The Therapeutic Goods Committee:**

   **(a) NOTES that the Therapeutic Goods Administration will be undertaking stakeholder consultation on proposed new arrangements for the export of medicines from Australia;**

   **(b) NOTES that further consideration of standards for export only medicine may be necessary as part of the proposed new arrangements; and**

**(c) REQUESTS that the Committee be kept informed of progress in the development of the new arrangements for the export of medicines from Australia.**

# BLOOD AND TISSUES

## STANDARDS FOR BLOOD, BLOOD COMPONENTS AND PLASMA FOR FRACTIONATION

The TGC was requested to advise on the adoption of the 14th edition of the European Directorate for the Quality of Medicines and Healthcare of the Council of Europe *Guide to the Preparation, Use and Quality Assurance of Blood Components* (the Guide) as the standard for blood components and plasma for fractionation in Australia. This proposal had been considered, and endorsed, by the TGC's Subcommittee on Biologicals at its first meeting, held on 23 July 2008.

Requirements in Australia for blood, blood components and plasma for fractionation were specified currently by the 11th edition of the Guide, as prescribed by Therapeutic Goods Order No. 74 *Standards for Blood Components* (TGO 74). However the Guide had been updated several times since the publication of the 11th edition, with the TGA contributing to the development of successive editions. The TGA proposed that TGO 74 be superseded by a new TGO which would adopt the 14th edition of the Guide.

The TGC received a summary document showing the changes that had occurred to the Guide in the transition from the 11th to 14th edition and was informed that the most significant change in the 14th edition was the increase in the maximum volume of plasma allowed to be collected by apheresis annually from 15 to 25 litres. The TGA viewed this change as being reflective of best practice, having potential to increase the collection of plasma in Australia and contribute to domestic supply of plasma derivatives.

The TGA also proposed that the new TGO would:

- formalise the exemption granted to an industry stakeholder under section 14/14A of the *Therapeutic Goods Act 1989* to allow the collection of blood from individuals with malignant disease or past history of malignancy, as comprehensive evidence had been provided showing that malignancy was not transmitted through donations from those who had recovered from malignancy; and
- continue the exception relating to tropical areas within Australia as needed for the 11th edition of the Guide, as the concern that certain diseases were endemic to tropical areas was not relevant to donors from tropical areas in Australia.

The TGC was informed that stakeholders had been consulted and provided comments during the drafting of the 14th edition of the Guide, and the major stakeholder also had assessed whether any areas of current Australian practice were at variance with the recommendations of the Guide. The conclusion was that there were no significant gaps between current practice and the requirements of the 14th edition of the Guide.

The Meeting discussed the statement contained in TGO 74, and intended to be carried forward into the new TGO, that blood and blood components must only be manufactured from blood that tests negative for HIV-1 and HCV Nucleic Acid Amplification Technology (NAT). The omission of HIV-2 was questioned, but it was advised that technology to test for HIV-2 was not as advanced as that for HIV-1. The meaning of a 'negative test' was also discussed as some Members considered

this to be an ill-defined term and a negative test only meant 'not detected' at the level of sensitivity of the test applied.

The TGC was informed however that the TGA assesses test methods and could intervene when a method was inappropriate. The TGA's preference therefore was that the TGO not include detailed information on test methods, but allow flexibility so that the most appropriate test method consistent with current technology could be used. International documents relating to the validation of NAT testing, which the TGA referred to in its assessments, were noted.

Given that the statement in question did not differ from that in TGO 74, there was only one sponsor to which the provision was relevant, the TGA assessed the test used by that stakeholder to ensure it was properly validated and of sufficient sensitivity, and there had been no public health issues arising from this in the past, the TGC accepted the wording proposed.

**RESOLUTION:**

**The Therapeutic Goods Committee RECOMMENDS:**

1. **the adoption of the 14th edition of the European Directorate for the Quality of Medicines and Healthcare of the Council of Europe document *Guide for the Preparation, Use and Quality Assurance of Blood Components,* dated 2008, Council of Europe Publishing, (the Guide) as the standard in Australia for blood, blood components and plasma for fractionation including red cells, white cells, platelets and plasma for transfusion.**

2. **that reference to tropical areas under the heading "tropical diseases" on page 65 of the Guide should not be taken to include areas within Australia.**

3. **that individuals with a malignant disease, or history of such, should not be permanently deferred from donation as specified on page 63 of the Guide.**

4. **that, as currently specified in Therapeutic Goods Order No. 74 *Standards for Blood Components*:**

    (a) **blood, blood components and plasma for fractionation must only be manufactured from blood that tests negative for HIV-1 and HCV using Nucleic Acid Amplification Technology; and**

    (b) **blood, blood components and plasma for fractionation must not be manufactured from blood donors who:**
    - **have lived in the United Kingdom for a cumulative period of six months or more between 1 January 1980 and 31 December 1996; or**
    - **have had a transfusion of blood or blood products in the United Kingdom from 1980 onwards.**

## UPDATE ON DEVELOPMENT OF A STANDARD FOR THE MINIMISATION OF INFECTIOUS DISEASE TRANSMISSION VIA HUMAN TISSUE BASED PRODUCTS

The TGC was informed of progress in the development of a standard relating to the minimisation of infectious disease via human tissue based products. This had been a matter considered by the Subcommittee on Biologicals at its meeting held on 23 July 2008, when an initial draft of an Order

was presented for review. The Order, when finalised, would be an overarching standard that would complement a number of tissue specific standards. Both the overarching standard and the tissue specific standards would be mandated as Therapeutic Goods Orders under the *Therapeutic Goods Act 1989*.

The TGC noted the importance of this standard for the new regulatory framework for human cells and tissue therapies and that the work was still in its early stages. However the TGA expected that the revised draft would be available by the end of the year. On that basis, the TGC anticipated the consultation being undertaken early in 2009, and the results of that being presented to the Committee for consideration in the first half of 2009.

**RESOLUTION:**

**The Therapeutic Goods Committee (TGC):**

1. **NOTES progress by the TGC's Subcommittee on Biologicals, and the Therapeutic Goods Administration (TGA), in preparing a draft standard for the minimisation of infectious disease transmission via human tissue based products.**

2. **NOTES that the draft standard draws on work previously undertaken by the TGA in conjunction with various working groups convened from the tissue banking sector.**

3. **NOTES that broad stakeholder consultation will need to be undertaken on the draft standard to ensure that all tissue banks are afforded the opportunity to provide comment.**

4. **RECOMMENDS that this consultation be undertaken at the direction of the Subcommittee, with stakeholder responses to be reviewed by the Subcommittee prior to consideration by the TGC.**

# MEDICAL DEVICES

No items.

# OTHER MATTERS

## THERAPEUTIC GOODS ORDER NO. 64 STANDARD FOR TAMPONS – MENSTRUAL – PROPOSED AMENDMENT TO ADOPT THE NEW STANDARD AS/NZS 2869:2008 TAMPONS MENSTRUAL

TGC advice was requested on a proposal to amend Therapeutic Goods Order No. 64 *Standard for Tampons – Menstrual* (TGO 64) to adopt the new Standards Australia standard AS/NZS 2869:2008 *Tampons Menstrual*. This edition of AS/NZS 2869 affected major changes to the way in which tampon absorbency was measured and removed the specific reference to the Toxic Shock Syndrome Information Service (TSSIS).

The TGC recalled that, in 2006, a stakeholder had made a submission to the Committee seeking an amendment to TGO 64 in order to permit the use of the EDANA/FDA absorbency test methodology. The TGC recommended that the stakeholder request Standards Australia to consider amending the test method given in AS/NZS 2869:1998 to incorporate the EDANA test methodology, noting however that any changes to AS/NZS 2869 should take into account implications for the labelling of tampons marketed in Australia. Standards Australia subsequently developed the new Standard AS/NZS 2869: 2008 *Tampons -Menstrual*, which adopted the EDANA/FDA absorbency test methodology as requested.

The TGC noted that both the new and the old test methods provided a reliable and accurate measure of tampon absorbency. Although the new test method took longer to perform and yielded a lower absorbency result than the old method, industry preferred the new method as it meant that the test method for measuring tampon absorbency would be the same world-wide. This would reduce the compliance burden on Australian tampon suppliers.

In view of the lower absorbency results obtained with the new test method, Standards Australia had made a consequential change to the part of AS 2869:2008 relating to labelling, so that labels on Australian tampons would remain the same as they were previously, avoiding any confusion among consumers.

It was noted that the other change in AS 2869:2008, removal of the specific reference to the Toxic Shock Syndrome Information Service (TSSIS), followed from a change from telephone line / PO Box services to a web-based service.

The TGC was advised that the TGA had been represented on the Standards Australia committee responsible for the development of AS/NZS 2869: 2008 and fully supported the update of TGO 64 to adopt this new edition of the Australian Standard. The TGA was currently seeking agreement from industry stakeholders to the amendment of TGO 64 to incorporate AS/NZS 2869:2008 as the standard for menstrual tampons in Australia.

The TGC supported the amendment of TGO 64, advising that the appropriate transition time would need to be determined in consultation with industry.

**RESOLUTION:**

**The Therapeutic Goods Committee:**

1. **NOTES that Standards Australia has developed a new tampons standard, AS/NZS 2869:2008 *Tampons Menstrual* which:**

   (a) **adopts a new absorbency test methodology, namely the EDANA/FDA methodology; and**

   (b) **updates the reference to the Toxic Shock Syndrome Information Service (TSSIS).**

2. **NOTES that the Therapeutic Goods Administration is currently consulting key industry bodies on the proposal to amend Therapeutic Goods Order No. 64 *Standard for Tampons – Menstrual*, as amended by Therapeutic Goods Order No. 64A, to adopt the new Australia New Zealand Standard AS/NZS 2869:2008 *Tampons – Menstrual*.**

3. **RECOMMENDS that, subject to industry agreement, Therapeutic Goods Order No. 64 *Standard for Tampons – Menstrual* is amended to adopt AS/NZS 2869:2008 *Tampons – Menstrual*.**

# CLOSE OF MEETING

The TGC agreed that the next Meeting of the Committee should be held in March 2009 and requested that Members be canvassed via email for their availability.

There being no further business, the Chair closed the Meeting at 4:00pm and thanked Members for their attendance.