EXPLANATORY STATEMENT

Therapeutic Goods Act 1989

Therapeutic Goods Order No. 78 *Standard for Tablets and Capsules*

OUTLINE

Therapeutic Goods Order No. 78 *Standard for Tablets and Capsules* ('TGO 78' or 'the Order') is an order made by the delegate of the Minister for Health and Ageing under section 10 of the *Therapeutic Goods Act 1989* ('the Act').

The Order supersedes an existing Therapeutic Goods Order [Therapeutic Goods Order No. 56 *General standard for tablets, pills and capsules* ('TGO 56'), made on 19 September 1996]. It introduces changes sought by the industry sectors, modernises requirements relating to the quality of tablets (but not including pills) and capsules, and is largely consistent with international standards, where such exist.

TGO 78 commences the day after it is registered on the Federal Register of Legislative Instruments ('FRLI') but includes a two year transition period until 1 November 2010 for medicines to achieve compliance with the provisions of TGO 78 rather than those of TGO 56.

BACKGROUND

Section 10 of the Act provides the Minister with the power to determine standards for therapeutic goods, or to amend or revoke existing standards, after consultation with a committee established by the Therapeutic Goods Regulations 1990 ('the Regulations') to advise the Minister on standards. The Therapeutic Goods Committee ('TGC') is the committee established by the Regulations for this purpose, and it is established by, and its functions and composition are set out in, regulation 34 of the Regulations.

Standards determined by the Minister under section 10 of the Act may be specified by reference to quality, procedures to be carried out in the manufacture of therapeutic goods, specified monographs or such other matters as the Minister thinks fit. In general, a medicine must not be imported, exported or supplied if it does not conform with standards applicable to that medicine unless excused in law. Paragraph (b) of subsection 10(2) of the Act states that an order establishing a standard for therapeutic goods may require that a matter relating to the standard be determined in accordance with a particular test.

The current standard for tablets and capsules is provided in TGO 56, made on 19 September 1996 (Legislative Instrument F2008B00045).

At its 31st meeting, held on 29 November 2007, the TGC advised by resolution that there was a strong justification to progress a revision to TGO 56. The TGC also recommended that stakeholder consultation be undertaken on a replacement standard.

Following consideration of stakeholder responses at its meeting on 29 April 2008, the TGC advised by resolution that draft TGO 78, as amended by the committee at that meeting, should be adopted as a standard for medicines determined under section 10 of the Act.

TGO 78 specifies the general minimum quality requirements for tablets and capsules that apply throughout the shelf-life of the medicine.

In particular, TGO 78 specifies that:

- a tablet or capsule that is the subject of an individual monograph in the British Pharmacopoeia must comply with that monograph, subject to certain qualifications;
- a tablet or capsule that contains 100 micrograms or more of folic acid must comply with the specified test for dissolution, subject to certain qualifications;
- a listed (necessarily, lower risk) tablet or capsule that is not subject to an individual British Pharmacopoeia monograph must comply with specific tests and limits regarding uniformity of weight, average content of active ingredient(s) or component(s), dissolution, disintegration and dispersion. The tests and limits vary with the type of tablet or capsule and the nature of the active ingredient; and
- a registered (necessarily, higher risk) tablet or capsule that is not subject to an individual British Pharmacopoeia monograph must comply with specific tests and limits regarding uniformity of dosage units, average content of active ingredient(s), dissolution, disintegration, and dispersion. The tests and limits vary with the type of tablet or capsule and the nature of the active ingredient.

TGO 78 does not apply to 'pills'. 'Pills' will continue to be subject to TGO 56 until its revocation on 1 November 2010. It is the intention of the Therapeutic Goods Administration ('TGA') to undertake consultation to determine if a new standard for pills is required prior to the revocation of TGO 56.

Under paragraph 6(d)(i) of the *Legislative Instruments Act 2003* ('LIA'), an instrument is a legislative instrument if it is declared to be a disallowable instrument under legislation in force before the commencement of the LIA. Section 12 of the Act provides that standards under section 10 and orders revoking, varying or modifying standards of that kind are disallowable instruments. Therefore, the Order is a legislative instrument and it is subject to tabling and disallowance in the Parliament under sections 38 and 42 of the LIA.

CONSULTATION

The development of TGO 78 followed from a review of the requirements for tablets and capsules undertaken by an expert committee in preparation for the proposed, but now postponed, Australia New Zealand Therapeutic Products Authority. Submissions previously made to the TGC and to the TGA suggesting revisions to TGO 56 were also taken into account.

Comprehensive stakeholder consultation was undertaken on a draft of TGO 78 in early 2008.

The stakeholder consultation process involved publication on the Internet site of the TGA <http://www.tga.gov.au> of a notice inviting comment together with the draft TGO 78 and a companion guidance document explaining the proposed requirements. Peak industry bodies, health professional organisations, consumer organisations and relevant areas of government

were directly invited to provide comment. The period allowed for submission of comments was approximately six weeks.

The consultation attracted 17 submissions, all of which were considered by the TGC at its 32nd meeting, held on 29 April 2008. Stakeholders were generally supportive of the draft TGO 78. Comments included:

- One stakeholder questioned the requirement for the demonstration of dissolution of folic acid from capsules, as this would require additional testing to be undertaken and some existing products were expected to not comply with this requirement. The TGC noted the public health initiatives to prevent neural tube defects, such as spina bifida, in unborn babies, by the consumption of folate (which is presented in medicines as folic acid) by the intending mother. The TGC did not support the stakeholder's challenge to the inclusion of subsection 9(2) in the Order.
- Several submissions argued that Schedule 1 should apply to registered tablets and capsules as well as to listed tablets and capsules. The TGC noted that the registration process for complementary medicines included individual assessment of limits for active ingredients, and that there would be opportunity for sponsors to seek exemption from the limits of TGO 78, where justified. The TGC did not support the stakeholders' request that subsection 10(b)(i) be replicated in section 11 of the Order.
- One stakeholder challenged the lower limits of 90% presented in Schedule 1, as the comparable limit in TGO 56 was 85% and the new requirement would entail additional testing or product reformulation. The TGC supported the 90% limits as these limits are consistent with international standards.

Compared to the consultation draft, the changes proposed by the TGC were considered to be minor or editorial in nature.

The delegate of the Minister for Health and Ageing has accepted the recommendation made by the TGC that draft TGO 78 be adopted as a standard determined under section 10 of the Act.

REGULATION IMPACT

Preliminary assessment of compliance costs associated with TGO 78, using the preliminary assessment form developed by the Office of Best Practice Regulation, has been undertaken in accordance with Best Practice Regulation requirements.

This preliminary assessment led to the conclusion that the Order would have a low impact on business and would not restrict competition. As the impact would be low, a Regulation Impact Statement has not been prepared.

TGO 78 is an instrument that is of a minor or machinery nature that does not substantially alter existing arrangements. The Order serves to modernise quality requirements that have been in place for over 10 years. The Order introduces a number of changes sought by the industry sectors. The Order is largely consistent with internationally harmonised standards, where such exist.

Sponsors who encounter difficulties complying with the requirements for a specific medicine can apply to the TGA for consent for non-compliance to the applicable requirement. Such applications for consent will be considered on a case-by-case basis.

REFERENCED DOCUMENTS

Information on the documents referred to in TGO 78 follows:

- The **Act** and **Regulations** may be viewed and downloaded from the ComLaw Internet site <http://www.comlaw.gov.au>, a link to which is presented on the TGA's Internet site <http://www.tga.gov.au>.

- **TGO 56** may be viewed and downloaded from the ComLaw or TGA Internet sites.

- The current definition of the ***British Pharmacopoeia*** under subsection 3(1) of the Act is the British Pharmacopoeia 2008. The British Pharmacopoeia 2008 is a collection of approximately 2900 monographs for pharmaceutical substances and medicinal products for human use. Monographs for tablets and capsules specify requirements for identification, assay (content of active ingredient), related substances (impurities), uniformity, dissolution, disintegration and other parameters. Associated test methods are also included in the British Pharmacopoeia. The British Pharmacopoeia is, generally, considered to be an essential reference for anyone concerned with the quality of medicines, including for the pharmaceutical and chemical industries, quality control personnel, analysts and academics. The British Pharmacopoeia is published by The Stationery Office, on behalf of the Medicines and Healthcare products Regulatory Agency of the UK. It is available for purchase in hard copy (ISBN-10: 0 11 322750 7) or soft copy (compact disc or online edition).

- The **United States Pharmacopeia 31st edition – National Formulary 26th edition** is a collection of approximately 4000 monographs for pharmaceutical substances and medicinal products for human use. Its content and role are similar to that of the British Pharmacopoeia. The United States Pharmacopeia – National Formulary is published by The United States Pharmacopeial Convention. It is available for purchase in hard copy (ISBN: 1-889788-53-8) or soft copy (compact disc or online edition).

- **Nutrient Reference Values for Australia and New Zealand Including Recommended Dietary Intakes** outlines the levels of intake of essential nutrients considered to be adequate to meet the known nutritional needs of practically all healthy people for prevention of deficiency states. The document was endorsed by the National Health and Medical Research Council on 9 September 2005 and published in 2006. It is available at no cost in hard copy (ISBN: 1864962372) or soft copy (online edition).

The meeting reports and resolution of the TGC's 31st and 32nd meeting referred to in this Explanatory Statement may be viewed and downloaded from the TGA's Internet site.

Attachment 1

TGO 78 – Description by Section

Execution page authorises the commencement of the Order and revocation, on 1 November 2010, of the current Therapeutic Goods Order No 56 *General requirements for tablets, pills and capsules* (TGO 56).

Section 1 specifies that the name of the Order is Therapeutic Goods Order No. 78 – *Standard for Tablets and Capsules.*

Section 2 specifies that the Order commences on the day after the day it is registered on the Federal Register of Legislative Instruments.

Section 3 specifies that up until 31 October 2010, medicines that are subject to TGO 78 must comply with either the requirements specified in TGO 78 or the requirements specified in TGO 56. Following the revocation of TGO 56 on 1 November 2010, only TGO 78 will apply to tablets and capsules to the extent that the Order operates.

Section 4 is an introduction to the Order. It states that the Order establishes the minimum quality requirements that apply to tablets and capsules throughout the shelf life of the medicine.

Section 5 provides definitions of terms used in the Order and, where relevant, directs the reader to meanings given in the Act or Regulations. Definitions provided in section 5 include: 'capsule', 'chewable tablet', 'dispersible tablet', 'effervescent tablet', 'enzyme', 'mineral', 'mineral compound', 'monograph', 'modified-release', 'pill', 'probiotic', 'provitamin', 'stated content', 'tablet, 'United States Pharmacopeia-National Formulary' and 'vitamin'.

The definitions of 'capsule' and 'tablet' include, by reference, the numerous types of capsules and tablets described in the British Pharmacopoeia. The definition for 'tablet' does not include 'pill'.

Section 6 describes the scope of application of the Order. Unless specifically exempted from the application of the Order or exemption has been granted by the Secretary under sections 14 or 14A of the Act, the Order applies to all tablets and capsules for oral administration to humans and that come within the operation of the Act.

Section 7 specifies a range of medicines that are not subject to the Order.

Section 8 specifies that a tablet or capsule that is the subject of a monograph in the British Pharmacopoeia must comply with that monograph. This requirement is qualified depending on whether the medicine is listed or registered in the Australian Register of Therapeutic Goods. (Note: Listed medicines are lower-risk medicines, e.g., vitamin, mineral or herbal medicines. Registered medicines are higher-risk medicines, e.g., prescription or pharmacy-only medicines).

Section 8(a) qualifies the above requirement for listed medicines, which need not comply with the test for Uniformity of Dosage Units and can instead comply with the less demanding requirements of the test for Uniformity of Weight.

Section 8(b) qualifies the above requirement for registered medicines. If the British Pharmacopoeia is silent regarding a test for dissolution, but such a test is applied by the monograph of the United States Pharmacopeia-National Formulary, then the tablet or capsule is required to comply with that United States Pharmacopeia-National Formulary dissolution test.

Section 9 specifies that a tablet or capsule containing 100 micrograms or more of folic acid must comply with specified dissolution requirements. The requirements differ for tablets and capsules, and if the folic acid is present in a tablet as a single active ingredient or with other active ingredients. The test methods and limits are as specified in the United States Pharmacopeia-National Formulary.

Section 10 specifies the tests with which a listed tablet or capsule must comply if there is no individual British Pharmacopoeia monograph for the tablet or capsule. Which tests apply to a listed tablet or capsule, and the limits that apply in the test, depend on the particular type of tablet or capsule (e.g., whether it is an effervescent tablet or a modified-release capsule) and the nature of the active ingredient (e.g., whether it contains folic acid or an oil-soluble vitamin).

Subsection 10(a) specifies that a tablet or capsule must comply with the British Pharmacopoeia's Uniformity of Weight test.

Subsection 10(b) specifies that the average content of each active ingredient or component in a tablet or capsule must be in the range 90-120% of the stated content. Some exceptions are made:

- Paragraph (i) replaces the 90-120% limits with the limits tabulated in Schedule 1 for ingredients of the types nominated in Schedule 1.

- Paragraph (ii) removes the 120% limit for a component in an active ingredient where the ingredient is of natural origin and there are two or more components and the proportions of these components vary independently.

- Paragraph (iii) removes any requirement to comply with limits on the average content for a multi-component ingredient for which no label claim is made for any component.

- Paragraph (iv) removes any requirement to comply with limits on the average content for an ingredient that is a homoeopathic ingredient.

Subsection 10(c) specifies that a modified-release tablet or capsule must comply with a suitable test for dissolution.

Subsection 10(d) specifies that where a dissolution test is not required then the tablet or capsule must comply with the relevant British Pharmacopoeia test for disintegration.

Subsection 10(e) specifies compliance with the British Pharmacopoeia's test for fineness of dispersion for a dispersible tablet.

Subsection 10(f) specifies that section 9 applies to listed tablets and capsules.

Section 11 specifies the tests with which a tablet or capsule, that is a registered good, must comply if there is no individual British Pharmacopoeia monograph for that tablet or capsule. Which tests apply to a tablet or capsule that is a registered good, and the limits that apply in the test, depend on the particular type of tablet or capsule (e.g., whether it is an effervescent or dispersible tablet) and the nature or the active ingredient (e.g., whether it contains folic acid or is an antibiotic).

Subsection 11(a) specifies that a tablet or capsule must comply with the British Pharmacopoeia's Uniformity of Dosage Unit test.

Subsection 11(b) specifies that the average content of each active ingredient in a tablet or capsule must be in the range 92.5-107.5% of the stated content. One exception is made:

> Paragraph (i) applies to antibiotic ingredients that are tested using a microbiological test. The paragraph uses the terminology appropriate to describe the precision of a microbiological test. The limits applied in this paragraph are comparable to those applied to other tablets and capsules.

Subsection 11(c) specifies which tablets and capsules must comply with a test for dissolution. If either the British Pharmacopoeia or the USP-NF require a dissolution test for a particular active ingredient, then a tablet or capsule containing that active ingredient must comply with a suitable test for dissolution. Dosage forms for which a dissolution test is not appropriate are excepted.

Subsection 11(d) specifies that where a dissolution test is not required then the tablet or capsule must comply with the relevant British Pharmacopoeia test for disintegration.

Subsection 11(e) specifies compliance with the British Pharmacopoeia's test for fineness of dispersion for a dispersible tablet.

Subsection 11(f) specifies that section 9 applies to tablets and capsules containing folic acid, that are registered goods.

Schedule 1 tabulates the limits for content of active component(s) or ingredient(s) in a tablet or capsule, that is a listed good. That Schedule must be read in conjunction with subsection 10(b)(i).