Australian Government
Department of Health
Therapeutic Goods Administration

Remaking Therapeutic Goods Order No. 78 - *Standard for Tablets and Capsules* and reintroducing pills into the remade Order

Consultation paper

Version 1.0, December 2018

TGA Health Safety Regulation

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Purpose

The Therapeutic Goods Administration (TGA) is seeking feedback on a proposed remade Therapeutic Goods Order for tablets, capsules and pills, based on the existing Therapeutic Goods Order No. 78 *Standard for Tablets and Capsules* (TGO 78, the Order).

Although TGO 78 continues to operate largely effectively and efficiently, it would beneficial to improve clarity on some requirements as well as create efficiency through increased international harmonisation. Accordingly, we are proposing to remake the Order under section 10 of the *Therapeutic Goods Act 1989* (the Act) to specify the physical and chemical quality requirements for tablets and capsules supplied in Australia.

Additionally the remade Order will reintroduce physical and chemical quality requirements for pills supplied in Australia.

Consideration is being given to making technical amendments to improve the efficiency of the Order and achieve the objectives for which it was initially required (to ensure it is fit for purpose).

Scope

The proposed remade Order incorporates the current requirements of TGO 78 and, in doing so, does not substantively alter existing arrangements. We are specifically seeking feedback on the suitability of the remade Order and any potential impact of proposed amendments on stakeholders.

The proposed amendments are outlined in this document and are detailed in a draft remade Order and draft guidance document.

Background

TGO 78 is the minimum quality standard for medicines that are tablets or capsules intended for oral administration. TGO 78 commenced on 7 November 2008. In accordance with the *Legislative Instruments Act 2003*, legislative instruments are automatically repealed after a fixed period of time (subject to some exceptions). This automatic repeal is called 'sunsetting'. TGO 78 is due to sunset on 1 April 2019.

In accordance with the Sunsetting legislative instruments guidance note, TGO 78 was assessed as to whether it is operating 'effectively and efficiently' when compared to no regulation in force.

Initial consultation with peak industry bodies has confirmed that the Order should be remade to provide continuing clarity on specific requirements needed to maintain quality standards for tablets and capsules.

TGO 78 has been reviewed in the context of amendments made to the Act, and updates to international standards, since its commencement in 2008. In its current form, it lacks alignment with the default standards recognised in the Act and also clarity on some technical requirements. The proposed changes seek to address these issues.

The sunsetting of TGO 78 presents an opportunity to update requirements to ensure that the Order is fit for purpose and aligned internationally where appropriate. The proposed

amendments should not be interpreted to imply that there are concerns with the general quality of medicines currently supplied in Australia.

Default standards in the Act

In July 2009, monographs in the European Pharmacopoeia (EP) and the United States Pharmacopeia – National Formulary (USP) were included as default standards in the Act, in addition to those in the British Pharmacopoeia (BP). However, TGO 78 was not similarly amended at that time. This has created challenges for some sponsors; that is, those whose medicines comply with one of the recognised pharmacopoeias for medicines supplied overseas but who must also apply specific requirements when the same goods are supplied in Australia. For example, manufacturing specifications stating compliance with the EP for supply in Europe do not comply with TGO 78 requirements as only the BP is recognised. The recognition of these pharmacopoeias in the Order will provide more options for sponsors, thereby reducing regulatory burden and improving international harmonisation.

Impurities

Ensuring the safety of therapeutic goods is critical and one of the key roles of the TGA.

Under the provisions of the Act, therapeutic goods must comply with applicable standards. For example, sponsors must ensure that their raw materials are of suitable quality, which includes ensuring compliance with limits for impurities such as heavy metals.

Under the current TGO 78, tablets and capsules with individual monographs in the BP must comply with the impurity limits included in that pharmacopoeia for those types of finished goods. However, requirements for impurities are not clear for tablets and capsules without an individual monograph.

To ensure consistency, and to provide safety assurances for consumers, requirements for impurities that will apply to all tablets, capsules and pills are being included in the remade Order.

Quality standard for pills

Therapeutic Goods Order No. 56 *General standard for tablets, pills and capsules* (TGO 56) preceded TGO 78. Assuring the quality of these discrete dosage forms is important to ensure that they deliver their intended therapeutic effect and to provide a measure of continuing consistency in performance over time.

Various categories of tablets are recognised dosage forms in Australian approved terminology for therapeutic goods; for example, coated tablets, uncoated tablets, effervescent tablets, modified release tablets, etc. Compressed lozenges, which are designed to dissolve or disintegrate in the mouth, are considered to be tablets.

Capsules can be hard or soft; the contents may be present as powders or liquids. Release of the active ingredients from capsules can also be modified in several ways, for example, enteric capsules.

Pills differ from tablets and capsules as they are manufactured using wet massing, piping and moulding techniques, not compression. They can be coated, but usually contain only certain limited excipient ingredients.

TGO 78 did not apply to pills, although the requirements for pills subject to TGO 56 were in force until 1 November 2010. The explanatory statement for TGO 78 noted that the TGA intended to undertake consultation to determine if a new standard for pills was required prior to the

revocation of TGO 56. This consultation did not occur and requirements for pills have been left with uncertainty since November 2010.

A review of medicines identified as 'pills' on the Australian Register of Therapeutic Goods (ARTG) has confirmed that these are all Traditional Chinese Medicines. It appears that, with the exception of the traditional medicine paradigms, this dosage form has been largely replaced by compressed tablets.

Proposed changes

International harmonisation

Recognition of default standards in the *Therapeutic Goods Act 1989*

The remade Order will offer sponsors a choice to stay with existing requirements, or to use requirements based on a default standard, as defined in the Act.

TGO 78 requires that medicines must meet the requirements of a relevant individual monograph in the BP, if one exists. In the absence of a BP monograph, Australian specific requirements are applied. This approach precludes sponsors from following either the EP or the USP. The proposed amendment to TGO 78 would allow sponsors of medicines made and supplied internationally to choose to comply with any relevant set of requirements, BP, EP, USP or Australian, to achieve the least regulatory burden.

Adoption of internationally-harmonised limits for impurities

Previously, the control of impurities in medicines was largely focused on quality controls placed on raw materials. Occasionally, specific impurity limits were included in the individual monographs for finished goods.

Recently the BP and USP both introduced heavy metal requirements into the general monographs for finished goods. These limits will apply to medicines citing compliance with an individual monograph in either of the pharmacopoeias. For consistency, it is proposed that suitable limits are included for all tablets, capsules and pills.

Addition of these limits to the existing TGO 78 requirements, to create updated Australian specific requirements, does not impose significant new regulatory burden on sponsors. Compliance can be established in a number of ways. For example, it may be appropriate to use results generated under existing testing requirements for impurities in raw materials rather than routine testing of the finished goods to demonstrate compliance.

Impurity limits for herbal preparations

The BP and the USP have used different approaches to determine acceptable elemental impurity levels. In particular, there is a considerable discrepancy between the BP Herbal Drugs monograph and the USP ⟨2232⟩ Elemental Contaminants in Dietary Supplements monograph. This may reflect the different legislative frameworks in which herbal medicines and dietary supplements are regulated in each jurisdiction.

In this consultation, we are seeking feedback on the most appropriate limits to apply to herbal-based medicines not following an individual monograph. Two proposed options are presented within the draft Order: option 1 – arsenic, cadmium, lead and mercury limits based on

those in the BP; and option 2 - arsenic, cadmium, lead, total mercury and methyl mercury from the USP.

Widening stated content limits within the Order

The remade Order proposes to increase the default content limits for medicines not following an individual monograph in the BP, EP or USP. These wider limits are aligned with internationally agreed limits.

Reintroduction of pills to the scope of the Order

The remade instrument will also reintroduce quality requirements for 'pills'. Modern granulation manufacturing processes, to produce tablets, have largely replaced pills, other than for traditional medicines. The proposed requirements for pills align with the general requirements for pills described in the Pharmacopoeia of the People's Republic of China but will not be limited to pills within the Traditional Chinese Medicine paradigm.

Pills differ from tablets and capsules as they are manufactured using wet massing, piping and moulding techniques, not compression. They can be coated, but usually contain only certain limited excipient ingredients and are typically manufactured and supplied as part of traditional medicine paradigms.

Various categories of tablets are recognised dosage forms in Australian approved terminology for therapeutic goods; for example, coated tablets, uncoated tablets, effervescent tablets, modified release tablets, etc. Compressed lozenges, which are designed to dissolve or disintegrate in the mouth, are considered to be tablets.

Capsules can be hard or soft; the contents may be present as powders or liquids. Release of the active ingredients from capsules can also be modified in several ways, for example, enteric capsules.

Application of the Order to unapproved goods

The requirements of TGO 78 apply to each medicine that is a tablet or capsule intended for oral administration and for human use and that comes within the operation of the Act. This means that it applies to medicines listed or registered on the ARTG and also to medicines not required to be on the ARTG ('unapproved goods'). The only exceptions are export only medicines, personal imports as described under Item 1 of Schedule 5 to the *Therapeutic Goods Regulations 1990* and radiopharmaceuticals.

Although TGO 78 applies to both approved and unapproved medicines, there is no specific mention of unapproved goods within the requirements. This lack of clarity will be addressed in the remade Order.

It is proposed that the remade Order applies only to medicines that are a tablet, capsule or pill intended for oral administration and on the ARTG (with the exceptions noted above). Requirements for unapproved medicines, such as extemporaneously compounded medicines and those used in clinical trials, would fall back to the default standards identified in the Act.

Implementation/Transition

The remade Order will allow sponsors to maintain compliance with existing requirements. Alternatively, they may choose to align with internationally-harmonised requirements as permitted in the Order at any stage. This means that a transition period is not required.

The remade Order reintroduces requirements for pills, as these have been absent since TGO 56 ceased in 2010. To allow sponsors sufficient time to ensure that their medicines comply with the new requirements for pills, these will commence on 1 April 2020.

Consultation

Specifically, the TGA is seeking feedback on the suitability and potential impact that any proposed amendments may have on affected stakeholders. Submissions must be relevant to the proposal to remake the standard for tablets and capsules and the reintroduction of pills. Submissions must be received by the closing date.

Submissions may include information on:

- how the reintroduction of pills to the remade Order will affect your business
- if the 12 month transition period for the inclusion of pills is suitable
- which impurity limits should apply to medicines not following an individual monograph
- how the introduction of heavy metal limits in the remade Order will affect your business
- the suitability of the requirements specified in the remade Order
- the exclusion of unapproved goods from the application of the remade Order
- the usefulness of the proposed guidance document
- suggested improvements to either document
- alternative options if you do not support the proposal
- an assessment of how the proposal will positively and adversely impact on you.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Scientific Operations Management Section – Scientific Evaluation Branch	14 December 2018

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