Australian Government

Department of Health and Ageing

Therapeutic Goods Administration

Guidance on Therapeutic Goods Order No. 80

Child-Resistant Packaging Requirements for Medicines

September 2008

Contents

General **3**

Explanation of sections **3**

Section 1 Name of Order 3

Section 2 Commencement 3

Section 3 Transition 4

Section 4 Introduction 4

Section 5 Interpretation 5

Section 6 Application 5

Section 7 Exemptions 6

Section 8 General requirements 7

Section 9 Reclosable packages 8

Performance requirements 8

Evidence of compliance with child and adult panel test requirements 8

Extrapolation of test results 9

Other evidence 9

Directions for opening and closing 10

Dropper applicators 10

Section 10 Non-reclosable packages 11

Schedule 1 Medicines to which this Order applies 11

Questions and answers relating to child-resistant packaging requirements **13**

Which expert committee is responsible for making recommendations on child-resistant packaging (CRP) requirements for medicines? 13

How do the requirements in this Order differ from the previous requirements? 13

Does the Order apply to the dispensing of medicines by pharmacists? 13

On what basis are substances included in Schedule 1 to the Order? 14

Why are class entries used in Schedule 1? 14

How are the class entries in Part 1 to Schedule 1 named? 14

What do class entries include? 14

What if my medicine contains a substance listed under a specific class, but is indicated for another use? 14

If a substance is included in Schedule 1, is CRP required for all pack sizes? 15

If a substance is included in Schedule 1, is CRP required for all dosage forms and presentations? 15

Will Schedule 1 be updated over time? 15

What sort of CRP can be used? 15

What is the status of CRP complying with superseded editions of Standards? 15

For reclosable CRP, does every combination of closure and container need to be tested? 16

Is non-reclosable packaging such as blister or strip packaging required to comply with any specified Standards? 16

Guidance on Therapeutic Goods Order No. 80

Child-Resistant Packaging Requirements for Medicines

This guidance document is intended to provide a plain English explanation of various requirements of Therapeutic Goods Order No. 80 *Child-Resistant Packaging requirements for Medicines* (TGO 80) and to give related information that will assist understanding, thereby facilitating compliance by sponsors. This document does not form part of the Order.

Unless otherwise indicated, the following guidance applies to both reclosable and non-reclosable forms of packaging.

General

The requirements of TGO 80 apply to medicines that come within the operation of the *Therapeutic Goods Act 1989* (the Act), Part 3-1 of which provides for the application of standards to therapeutic goods.

Such standards may relate to any matter relevant to the quality, safety or efficacy of a medicine, and generally, a medicine must not be imported, exported or supplied if it does not conform to an applicable standard.

Paragraph (c) of subsection 10(2) of the Act states that an Order establishing a standard for therapeutic goods may require that therapeutic goods, or a class of therapeutic goods identified in the Order, be labelled or packaged in a manner, or kept in containers that comply with requirements, specified in the Order.

TGO 80 is a standard that requires certain medicines to be packaged in a particular manner, i.e. with packaging that is child-resistant.

However, compliance with TGO 80 does not negate the need to comply with other packaging requirements that may apply under therapeutic goods legislation or other law, such as poisons and/or dangerous goods legislation.

Responsibility for compliance with the requirements of TGO 80 rests with the sponsors of the medicines to which the Order applies. It is not the responsibility of the packaging manufacturer unless that manufacturer is also the sponsor of the medicine.

Explanation of sections

The following sections explain the various sections of TGO 80.

Section 1 Name of Order

This section states the legal title of the Order.

Section 2 Commencement

This section states when the Order will commence to have effect.

This is specified as the day following the day on which the Order is registered on the Federal Register of Legislative Instruments (FRLI - http://www.frli.gov.au) which is the official repository of Commonwealth legislative instruments.

TGO 80 was registered on the FRLI on 5 September 2008 and therefore took effect on 6 September 2008.

Transition arrangements providing the timeline for compliance with TGO 80 are given in the following section.

Section 3 Transition

This section provides the date by which medicines must comply with TGO 80. This date is 1 September 2010.

Until 1 September 2010, sponsors have the choice of complying with either TGO 80, or its predecessor – Therapeutic Goods Order No. 65 *Child-Resistant Packaging for Therapeutic Goods* (TGO 65).

The same transition timeframe applies to both existing products and new products.

Stock that is released for supply/sale by a sponsor on and after 1 September 2010 will be subject to this Order. Stock that has been released for sale/supply (e.g. to warehouses, retailers and consumers) prior to 1 September 2010 will not be subject to this Order.

Sponsors should consult the guidelines for prescription medicines, OTC medicines, registered complementary medicines and listed complementary medicines for information about notification or approval processes for packaging changes that are consequent upon the requirements of a new Therapeutic Goods Order.

Section 4 Introduction

This section is included in the Order for information purposes. It does not contain any mandatory provisions, but provides information on:

- The objective of the Order: to help ensure that the packaging of medicines which may be significantly toxic to children if accidentally ingested is designed to be resistant to opening by children;
- The role of child-resistant packaging (CRP) in reducing the incidence of accidental poisoning in children and the distinction between child-resistant and child-proof;
- The nature of considerations typically taken into account by the relevant expert advisory committee in making recommendations on requirements for CRP, with six specific criteria listed; and
- The forms of packaging permitted by the Order and the intention to develop a best practice guideline on non-reclosable packaging that will assist sponsors to improve the robustness of blister or foil strip packaging and thus further reduce the potential for the accidental poisoning of children.

Specification of the criteria to be used for determination of a requirement for CRP is intended to provide greater transparency and accountability and contribute to consistency in decision making. Taken together, the criteria provide a framework for risk assessment. These criteria also will assist regulators and sponsors in being proactive in considering CRP requirements for any new therapeutic substances.

Section 5 Interpretation

This section provides definitions of terms used in the Order and where relevant, directs the reader to meanings given in the Act or its regulations.

The definition given for the term 'child-resistant packaging' (CRP), which is used in the title of the Order and throughout the Order, reflects the meaning given to this term in the various national or international Standards listed in subsection 9(1). It recognises that child-resistance is associated with a package as a whole rather than any individual component of the package such as a closure or a bottle, and that testing protocols for child-resistance necessarily involve a complete package. The definition also recognises the need for adults to be able to open the packaging easily and properly reclose it.

The term 'young children' used in the definition of 'child-resistant packaging' should be taken to mean children within the age group specified in the protocols given in the Standards referred to in subsection 9(1) for the testing of child-resistance. This age group is 42 to 51 months inclusive. While CRP is likely to provide benefits for children of other ages, testing of packaging in accordance with the protocols given in the Standards referred to only establishes the performance of the packaging in children of the stated age range.

Section 6 Application

This section specifies which medicines must be packaged in CRP. It specifies that the Order only applies to medicines for human use (as medicines solely for use in animals are regulated by the Australian Pesticides and Veterinary Medicines Authority under separate legislation) and that the requirements apply to the sponsor's original pack.

The section refers to lists of substances and classes of substances which, if present as an ingredient in a medicine, result in an obligation on the sponsor to ensure that the packaging is child-resistant and complies with the performance and other requirements of the Order unless otherwise exempted (refer to section 7).

Subsection 6(1) specifies that CRP requirements apply to:

- Any registered medicine that contains as an ingredient any substance belonging to a class specified in Part 1 to Schedule 1 of the Order; and
- Any registered medicine that contains as an ingredient any substance specified in Part 2 to Schedule 1 of the Order; and
- Any listed medicine that contains as an ingredient any substance specified in Part 2 to Schedule 1 of the Order; and
- Any other medicine which is presented in such a way that implies that the packaging is child-resistant.

Although CRP is not mandatory unless the medicine contains a substance specified in Schedule 1, the last point means that, if the presentation of a medicine is such that consumers could reasonably believe that the packaging is child-resistant, then the performance requirements of TGO 80 apply.

Presentations considered to imply child-resistance include closures with graphics typically used on child-resistant closures, for example, push down and turn graphics, and label statements or other product information referring to the package as being child-safe or preventing access by children.

The use of class entries in Part 1 to Schedule 1 imposes an automatic requirement for CRP on any registered medicine containing any new substance falling into any of the classes shown. However, requirements for CRP are independent of the approved indication(s).

On occasion, classes may include substances with dissimilar toxicity. Therefore, in some cases, entries in Part 1 to Schedule 1 may exclude specific substances – for example, pholcodine is excluded from the class 'Opioids'.

Part 2 to Schedule 1 lists specific substances (rather then classes of substances) that require CRP. Entries in Part 2 to Schedule 1 may be limited to specific concentrations or amounts of the particular ingredient above specified levels, or may exclude specific pack sizes or types.

Subsection 6(2) of the Order indicates that individual exemptions from the requirements of the Order can be granted by the Secretary in accordance with sections 14 and 14A of the Act. Those sections of the Act relate to approvals for the supply, importation or export of a medicine which does not conform to an applicable standard, such as this Order or parts of this Order.

Section 7 Exemptions

This section of TGO 80 describes a number of circumstances in which, or types of medicine to which, the requirements of the Order do not apply, notwithstanding that the medicine may contain a substance listed in Schedule 1.

In general, the medicines to which the requirements of the Order do not apply are ones for which the risk of accidental ingestion by children is low.

Some presentations may be difficult for a child to open or to access the contents (e.g. injections, spray presentations meeting specified criteria, and small containers with restricted flow inserts) or it may be difficult to ingest significant quantities (e.g. creams and ointments, and individually wrapped powders).

The exemption given in paragraph (d) of section 7 applies to medicines that are either solid or semi-solid AND are intended for application to the skin or mucous membrane. This would include, for example, creams, ointments, sticks and dusting powders for external application. Solid dosage forms such as tablets and capsules, which are not for application as specified, are excluded from this exemption.

Transdermal patches are specifically mentioned in paragraph (d) as being exempt. This is because the individual sachets used for packaging of transdermal patches would already meet the requirements of TGO 80 for non-reclosable packages. Furthermore reports of poisonings associated with transdermal patches indicate that the time of access generally is after use, rather than before use (i.e. accidental poisonings are associated with discarded patches rather than breaches of the original packaging).

Other exemptions in section 7 are based on there being minimal availability of the medicine to children (e.g. medicines not at their final stage of manufacture including bulk finished tablets which are still to be packaged, medicines only for use in a hospital setting or bulk medicine packs which are only supplied to a pharmacy for breakdown into smaller packs during dispensing for individual patients).

The exemption for bulk medicine packs is based on the exemption previously included in TGO 65 for containers 'holding 500 solid dosage units or more (excluding goods packed and labelled for retail supply)'. The exemption has been revised to provide more flexibility in the size of bulk medicine packs destined for dispensing use and also to provide an exemption for bulk packs of liquid preparations.

In relation to medicines that are starting materials used in the manufacture of another medicine, paragraph (i) exempts these unless the starting material is pre-packaged for supply without further formulation or is formulated into a dosage form. This means that active ingredients and excipients intended for use in the manufacture of medicines are exempt. However, if the same ingredient is pre-packaged ready for sale it is not exempt. For example, an ingredient such as eucalyptus oil can be used in manufacture of medicines, in which case it is exempt from these requirements; alternatively it can be pre-packaged for sale to the public, in which case it is not exempt.

Medicines that are solely for export will need to comply with the standards imposed by the importing country. Such medicines are therefore exempted from the requirements of TGO 80 by paragraph (l).

No specific exemption has been included in TGO 80 for medicines repackaged by a pharmacist during dispensing to meet the needs of individual patients who may experience difficulty in opening medicines with CRP. This is because the Order applies to sponsors of medicines and specifies requirements for the sponsor's original pack (see 'Application'). Although TGO 80 should help pharmacists in selecting appropriate packaging when a medicine cannot be dispensed in the sponsor's original pack, or the original pack is not appropriate for a particular patient, the repackaging of medicines by a pharmacist to meet individual patient needs is a matter of professional practice, which is not directed by this Order.

No specific exemption has been included for medicines intended solely for use in animals as the scope of the Order is limited to medicines for human use (see explanation under 'Application'). However medicines for human use which have incidental use in animals must comply with the requirements of the Order.

Section 8 General requirements

This section specifies a number of general requirements applying to CRP. Unless otherwise specified, these requirements apply to both reclosable and non-reclosable forms of CRP and are specified in this Order to ensure their uniform applicability to CRP complying with any of the nominated Standards.

The requirements of this section relate to fitness for purpose, retention of child-resistant properties, and compatibility between the material of the package and its contents, as well as the requirement that sight, unusual strength or unusual dexterity not be needed by adults to access the contents of the package.

The meaning of fitness for purpose extends beyond the general concept of suitability of the package (including its material of construction) for use with medicines, to include consideration of the child-resistant properties of the package.

A distinction between the shelf-life of the medicine and its in-use life is made. Shelf-life relates to the expiry dating of the medicine and CRP must retain its integrity and functionality for the duration of this period. In-use life refers to the number of times the package will be opened (e.g. to remove doses) before the contents are completely used. The particular CRP chosen for use must be able to withstand at least this number of openings and closings (if a reclosable container) or removal of all individual doses (if a non-reclosable container) without any deterioration in the child-resistant characteristics or performance.

The requirement that performance of the child-resistant feature not be adversely affected by the contents of the package is most relevant to reclosable packages containing liquids as some

plastics are known to be incompatible with particular hydrocarbons and there is evidence that this incompatibility can cause failure of an otherwise child-resistant closure. In other cases, the performance of a closure can be compromised by liquid contents which are sugary/syrupy, as crystals or a layer of the liquid may be deposited around the mouth of the bottle with repeated use.

Section 9 Reclosable packages

This section of the Order specifies the required performance standards that reclosable forms of CRP must meet and the need for sponsors to hold evidence of satisfactory performance.

Performance requirements

The performance standards for reclosable packages are based on compliance with the type testing requirements of any one of five nominated national or international Standards. These Standards are listed in subsection 9(1) of the Order.

Inclusion of the range of national or international Standards is intended to facilitate the use of packaging originating overseas, and to minimise the need for involvement of children in testing.

Although there are minor differences between Standards from different organisations, the key parameters of the child panel tests (ages of children and pass/fail criteria) and adult panel tests (ages and pass/fail criteria) are consistent. Therefore compliance with any one of these Standards is considered to provide equal assurance that a package, when type tested according to the Standards, meets an acceptable level of child-resistance and ease of use for adults.

There is no order of precedence for the Standards nominated - all are accepted with equal standing and if compliance with an overseas Standard is established, testing in accordance with the nominated Australian Standard is not required.

The age group tested in the child panel tests of the nominated Standards is specified as 42 to 51 months of age. Although this age group is at the high end of the age range at which child poisoning is most common, it is deliberately chosen in the Standards in order to challenge the packaging with children most likely to have the dexterity to succeed. While packaging that complies with the requirements of any of the Standards can be expected to be difficult for children of other ages to open, the ability of children outside the given age range to open the package is not tested and thus cannot be assumed.

It should be noted also that 'child-resistant' is not synonymous with 'child-proof' and that compliance of a package with any of the nominated Standards does not mean that all children included in the test group were unable to open the package or gain access to the contents.

Evidence of compliance with child and adult panel test requirements

Where CRP is required and a reclosable form of CRP is used, subsection 9(2) requires the sponsor to hold, and be able to submit upon request, documentation establishing that the package complies with at least one of the nominated Standards.

Depending on the level of assessment of the medicine, this evidence may or may not routinely be requested during the evaluation process or post-market review. Although listed medicines do not undergo an evaluation process, the obligations of sponsors of listed medicines in relation to compliance with TGO 80 are no different to those of sponsors of registered medicines. At the time that an application for listing is submitted, sponsors must

certify that the medicine conforms to every applicable standard, including that relating to CRP.

In most cases the requirement for evidence will be satisfied by a copy of a certification or test certificate issued by a recognised test agency[1] that is accredited to conduct, or has an established reputation in, testing of packaging for child-resistance, with sufficient information to establish that the package intended for use is the package tested. On occasions, particularly for packaging manufactured in Australia or New Zealand, sponsors may hold actual test data establishing compliance. This is acceptable but, as with certifications, it should be clearly demonstrable that the data apply to the package intended for use.

Extrapolation of test results

Extrapolation of test results refers to situations where the results from testing one combination of container and closure are taken to apply to a combination of container and closure of the same design but of different size, shape and/or neck diameter, in order to establish compliance with a Standard by analogy.

Many of the nominated Standards permit extrapolation of test results over a range of similar packages [e.g. over a range of closure (neck diameter) or container sizes] provided all other characteristics of the package remain the same. For example, if a series of containers differ only in capacity and the closures are identical, the International Standards Organization Standard ISO 8317:2003 requires testing only on the largest and smallest container sizes. Extrapolation of results from one package to another in a series to the extent permitted by the nominated Standard chosen for test is acceptable for the purposes of compliance with this Order.

Other evidence

For reclosable packages, subsection 9(3) requires that sponsors hold evidence to demonstrate that the general requirements for retention of fitness for purpose (for the shelf-life of the medicine) and retention of child-resistant properties (for the expected in-use life of the medicine), and for the contents not to adversely affect the performance of the child-resistant feature, are met. Ideally this evidence should be generated during packaging validation - it is not required for each batch produced although continuing compliance of components with specifications should be verified through normal quality control checks in accordance with usual GMP procedures.

It is not the intention of subsection 9(3) to necessitate child panel testing that is additional to that of a national or international Standard. However an absence of reported failures of the child-resistant feature is insufficient evidence to establish that subsection 9(3) is satisfied.

Compatibility of container/closure materials with the contents of the package is particularly relevant to liquid formulations. Considerable general information on the compatibility of materials used for containers and closures with particular formulation types and ingredients (e.g. aqueous bases, hydrocarbons, oils, syrups etc.) may be available from packaging manufacturers. Sponsors also should be able to establish simple laboratory test protocols

[1] Examples of recognised testing agencies accredited to conduct, or having an established reputation in, testing and certification of packaging for child-resistance include the Belgian Packaging Institute (Belgium), Burford Research Consultants (UK), Cambridge Materials Testing Limited (Canada), Child Related Research Inc. (USA), Great Lakes Marketing (USA), Institut Verpackungsmarktforschung (Germany), Laboratoire National D'Essais (France), Perritt Laboratories (USA) and Sunbeam Packaging Services (USA). Other agencies may be equally able to undertake testing for child-resistance.

specific to each combination of container content or formulation type and packaging material to demonstrate that, over time, the contents do not adversely affect (e.g. deform or weaken) the material of the package.

Demonstration of retention of fitness for purpose over the shelf-life of the medicine may involve the inclusion of an additional test(s) or observations in the initial (or later) stability programs, to verify that at specified times throughout the shelf-life of the medicines that the closure has not visibly deteriorated, it cannot be removed without the specific child-resistant mechanism being disengaged but can be removed easily by undertaking the specified action and can be properly reclosed without undue difficulty, and the application torque, if relevant to the closure type, remains within the specified range.

Retention of child-resistant properties for the expected in-use life of the medicine could be demonstrated through simulated in-use scenarios involving at least the number of pack openings and closings necessary for all doses of medicine within the package to be withdrawn, at the appropriate dose interval for the medicine.

As changes in specification (including changes in materials or method of manufacture) for any component of the package may affect performance, subsection 9(4) requires sponsors to hold evidence that any such changes made do not compromise child-resistance. A change to the material used for the wad or liner, or inclusion or removal of a wad or liner, may vary the package description sufficiently to warrant complete panel testing.

Subsection 9(5) specifies the additional evidence that sponsors should obtain to ensure that the expected child-resistant performance of the selected package is achieved and maintained during the packaging processes. The application of this information should be reflected in routine quality control testing.

The requirement of paragraph 9(5)(a) for sponsors to hold information on the types and sizes of container to which a specified closure may be applied relates only to those containers of immediate relevance to the sponsor's range of medicines, and not all possible combinations of packaging components. However it is not adequate for a sponsor to only hold information supporting the use of a closure with one particular container if the closure is likely to be used across a range of different container types and sizes.

Directions for opening and closing

As failure of reclosable forms of CRP can occur when closures are not adequately tightened or re-fastened, subsection 9(6) requires that any reclosable CRP include on it adequate directions for both opening and closing. These instructions may appear in the form of words or graphics on the package itself, or be conspicuously placed elsewhere on the label. Any written instructions must appear in the English language. The addition of this information in other languages is not prohibited.

Dropper applicators

Subsection 9(7) requires that droppers or applicators that are supplied in a package with medicines requiring CRP and which may be left in place on the container, in place of the original closure, once the goods are in-use also comply with the performance requirements of this Order. Goods commonly presented in this way include minoxidil lotions and paracetamol infant drops.

This requirement aims to ensure that the convenience of leaving a dropper or applicator in the container of medicines warranting CRP does not compromise child-safety throughout the in-use life of the goods.

Section 10 Non-reclosable packages

This section specifies the requirements for non-reclosable forms of packaging such as blister and strip packaging which, once opened, is not capable of being re-closed to its original form.

Unlike the requirements for reclosable forms of CRP, current requirements for non-reclosable packaging do not involve performance testing with child and adult panels. Instead the requirements are based on design and specified materials of construction.

Section 4 *Introduction* to this Order advises that the requirements applying to non-reclosable packaging reflect those of the Australian Standard AS 1928-2001 *Child-resistant packages* which remains current for non-reclosable packages (the scope of AS 1928-2007 is limited to reclosable packages).

However sponsors should be aware that, as stated in the *Introduction* to TGO 80, although this form of packaging has been accepted to date as providing a child-barrier, it is intended that a best practice guideline on non-reclosable packaging will be developed in order to assist sponsors to improve the robustness and effectiveness of blister or foil strip packaging and thereby further reduce the potential for accidental childhood poisoning from medicines packaged in this way.

Schedule 1 Medicines to which this Order applies

This Schedule to the Order identifies those substances and classes of substance which, if present in a medicine, necessitate that the medicine has CRP unless a general exemption exists under section 7 or a product-specific exemption has been granted under section 14 and 14A of the Act.

The principles governing the determination of substances to be included in Schedule 1 are explained in the *Introduction* to the Order.

Schedule 1 consists of three parts:

- Part 1, which specifies the classes of substance that, when any member of the class is included in a registered medicine, result in the requirements of the Order applying to the medicine. Examples of substances falling within each class are shown in the Schedule but sponsors should recognise the possibility that not all substances in any particular class are named;
- Part 2, which identifies a number of individual substances that do not readily fall within any of the classes named in Part 1 but which, when present in either a listed medicine or a registered medicine, result in a requirement for CRP. The Schedule entry may relate only to concentrations or amounts above specified levels, or exclude specific pack sizes or types; and
- Part 3, which provides an alphabetical listing of all substances and classes of substance included in Part 1 and Part 2 to Schedule 1, including the named examples of substances from each class given in Part 1. Part 3 is provided for cross-reference purposes, and will not necessarily show every substance in every class for which CRP is required.

The classification of substances in Part 1 is consistent with the Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization Collaborating Centre for Drug Statistics Methodology (http://www.whocc.no/atcddd/).

Each class listed in Part 1 includes all substances included under the given ATC classification (whether or not the substance is shown in the Schedule as an example of substances included

in the particular class), irrespective of the indication(s) included on the Australian Register of Therapeutic Goods for the medicine, unless the substance is specifically exempted from the Order.

On occasion, classes may include substances with dissimilar toxicity. Therefore in some cases, entries in Part 1 to Schedule 1 may exclude specific substances. For example, doxycycline is excluded from the class 'Antimalarials'.

The list of examples shown against each of the named classes is not exhaustive and new substances may appear in any class over time. As a consequence, if a new substance that falls into any of the classes listed is marketed, then registered medicines containing that substance will be required to have CRP unless a general exemption exists under section 7 for the particular dosage form or a specific exemption is granted under sections 14 and 14A of the Act.

Questions and answers relating to child-resistant packaging requirements

Which expert committee is responsible for making recommendations on child-resistant packaging (CRP) requirements for medicines?

Section 10 of the *Therapeutic Goods Act 1989* provides the Minister for Health and Ageing with the power to determine standards for therapeutic goods, or to amend or revoke existing standards, after consulting with respect to the proposed action with a committee established by the regulations to advise the Minister on standards.

The Therapeutic Goods Committee is the committee established by the *Therapeutic Goods Regulations 1990* to advise the Minister on standards.

Therapeutic Goods Order No. 80 *Child-Resistant Packaging Requirements for Medicines* has been made following consideration of advice provided by the Therapeutic Goods Committee.

Under existing legislation, the Therapeutic Goods Committee would also be requested to advise on any future changes to CRP requirements.

How do the requirements in this Order differ from the previous requirements?

Subject to the specified transition arrangements, TGO 80 supersedes Therapeutic Goods Order No. 65 (TGO 65) *Child-Resistant Packaging for Therapeutic Goods*. The main differences for sponsors are that TGO 80:

- updates the references to the ISO, British and Australian Standards for reclosable forms of CRP to refer to the current editions of those Standards;
- requires compliance of reclosable packaging with the test protocols given in at least one of the specified Standards rather than allowing the use of packaging previously accepted on the basis of compliance with older editions of Standards or other considerations (i.e. the Order no longer includes a Schedule specifying individual closures that are permitted for use based on historical information);
- identifies some additional substances or classes of substance for which CRP is required;
- clarifies the general exemptions and extends these to include some additional product types or circumstances; and
- includes for information the criteria to be considered by the relevant expert committee in making future recommendations relating to CRP requirements.

Does the Order apply to the dispensing of medicines by pharmacists?

TGO 80 is an Order is made under section 10 of the *Therapeutic Goods Act 1989*. However, section 6 of the Order limits its application to medicines supplied by a sponsor. This means that the requirements of TGO 80 apply to the sponsor's original pack.

TGO 80 does not specify the type or standard of packaging to be used by a pharmacist during dispensing where the original pack is not appropriate for a particular patient, or the quantity to be supplied does not match that contained in the original pack.

Although TGO 80 should help pharmacists identify medicines which should have CRP, and the standard of packaging expected of a sponsor, the repackaging of medicines by a

pharmacist to meet individual patient needs is a matter of professional practice and is not directed by this Order.

On what basis are substances included in Schedule 1 to the Order?

The criteria and principles intended for use in determining which substances warrant CRP are stated in the *Introduction* to the Order.

Preparation of Schedule 1 took into account submissions made by health departments and injury prevention agencies, information from Poisons Information Centres in Australia and the knowledge and experience of expert committee members.

Schedule 1 reflects the agreement that all substances with high toxicity should be included, even if these are ingredients of products that have infrequent use.

Why are class entries used in Schedule 1?

The use of class entries has the advantage of automatically requiring CRP for new drugs within any of the named classes. It provides consistency in requirements for all substances within the class, and clarity on packaging expectations for both industry and the regulator early in the application / evaluation process. It also contributes proactively to the identification of substances which may potentially be toxic to children if accidentally ingested.

How are the class entries in Part 1 to Schedule 1 named?

Classes included in Part 1 to Schedule 1 are named according to the Anatomical Therapeutic Chemical (ATC) classification system of the World Health Organization Collaborating Centre for Drug Statistics Methodology (http://www.whocc.no/atcddd/).

What do class entries include?

Each class includes all substances included under the given ATC classification on the WHO website, whether or not the substance is shown in the Schedule as an example of substances included in the particular class and irrespective of the indication(s) included on the Australian Register of Therapeutic Goods for the medicine.

As substances currently exempt from CRP requirements due to dose form or presentation may be marketed in new dose forms or presentations in the future, each class entry includes for reference purposes as complete a list as possible of substances within that class.

On occasion, classes may include substances with dissimilar toxicity. Therefore in some cases, entries in Part 1 to Schedule 1 may exclude specific substances.

What if my medicine contains a substance listed under a specific class, but is indicated for another use?

Requirements for CRP are independent of indication. Therefore, any substance named in Part 1 of Schedule 1 under a specific class is required to have CRP (unless a general exception exists for the dose form, particular presentation or circumstances) even if registered for an indication not consistent with the class under which the substance has been named.

If a substance is included in Schedule 1, is CRP required for all pack sizes?

Yes unless the relevant entry is in Part 2 to Schedule 1 AND it specifically mentions exemptions for particular pack sizes. The intent of TGO 80 is that if a substance is marketed in any pack size that meets the criteria given in the *Introduction*, then every pack size of medicine containing that substance requires CRP. Only with rare exception does the Order differentiate between products containing the same substance on the basis of pack size.

If a substance is included in Schedule 1, is CRP required for all dosage forms and presentations?

No. Section 7 of the Order gives a number of general exemptions from CRP requirements. These exemptions are based on the assessment that some dose forms, presentations or circumstances of use are associated with a reduced risk of accidental ingestion of the product by children, or there being minimal availability of the product to children. For example, dose forms such as injections, products not at their final stage of manufacture and products only used in hospitals or nursing homes would all have minimal availability to children and are exempted. Sponsors should check the exemptions detailed under section 7.

Will Schedule 1 be updated over time?

Yes. A proactive approach to the identification of substances which may present a hazard to children, and which therefore warrant CRP, is considered essential. It is therefore intended that the Therapeutic Goods Committee will review, on an annual basis, the need for new substances to be packaged with CRP, and any new information relevant to the potential hazard presented by existing substances. Stakeholders will be invited to provide submissions at the appropriate time.

What sort of CRP can be used?

The selection of appropriate CRP rests entirely with the sponsor and should take into account normal packaging considerations such as stability and maintenance of product quality and suitability for the intended target population.

If reclosable CRP is used, it must comply with at least one of the national or international Standards nominated in section 9 of the Order and the sponsor must satisfy themselves that this is the case and must hold evidence that establishes this. The selected CRP must also comply with the remaining requirements of section 9 and the general requirements specified in section 8 of the Order.

Unlike TGO 65, TGO 80 does not include a list of specific closures and containers that are accepted as meeting the requirements of the Order.

If non-reclosable packaging such as blister or foil strips is used, that packaging must comply with the requirements of section 10 of the Order as well as the general requirements specified in section 8.

What is the status of CRP complying with superseded editions of Standards?

Under this Order, the use of reclosable CRP complying with superseded editions of the nominated Standards will not be adequate because of the concern that such packaging may not perform as well as packaging meeting the requirements of more contemporary Standards.

Therefore during the transition period for the Order, sponsors using such CRP will need to either obtain evidence of certification against the specified editions of the nominated Standards or move to packaging systems for which such certification exists.

Where a specified edition of a Standard differs only in relation to one of the panel tests (for example, the adult panel test) then conduct of only that one panel test would be sufficient to bridge the gap and the results of the alternate panel test (i.e. the child panel test) undertaken in accordance with the previous edition of the Standard would remain valid.

For reclosable CRP, does every combination of closure and container need to be tested?

No. In many cases, where testing in accordance with a Standard has been conducted on one combination of container and closure, the nominated Standard permits extrapolation of the results to a range of container and/or closure sizes. The TGA will accept extrapolation within the parameters set in the nominated Standards.

Is non-reclosable packaging such as blister or strip packaging required to comply with any specified Standards?

Non-reclosable packaging must comply with the requirements given in section 10 of the Order. At the present time, these requirements are based on design and specified materials of construction and do not involve performance testing with child and adult panels.

However, sponsors are advised that it is intended that a best practice guideline on non-reclosable packaging will be developed by TGA in conjunction with industry in order to assist sponsors to improve the robustness and effectiveness of blister or foil strip packaging as a child barrier, and thereby further reduce the potential for accidental childhood poisoning from medicines packaged in this way.

Mandatory compliance with available Standards for assessing the child-resistance of non-reclosable packaging may be considered in the future.

Can exemptions from the requirements of TGO 80 be approved?

Yes. Subsection 6(2) of the Order indicates that individual exemptions from the requirements of the Order can be granted by the Secretary in accordance with sections 14 and 14A of the Act. Those sections of the Act relate to approvals for the supply, importation or export of a medicine which does not conform to an applicable standard, such as this Order or parts of this Order. Such approvals may be granted unconditionally or subject to conditions, and can relate to one batch or all batches of a medicine.

Where exemption from any aspect of this Order is sought, the sponsor should apply in writing to the Therapeutic Goods Administration (TGA), stating precisely the particular section or sections of the Order against which the exemption is sought, and providing justification for the exemption. When an exemption is granted, information concerning the exemption is published in the Commonwealth Government Notices Gazette.

However as the requirements of this Order are intended to contribute to reducing the incidence of accidental poisoning in children, sponsors should be aware that exemptions will only be considered where it can be established that the exemption sought will not compromise safety, or exceptional circumstances otherwise exist.