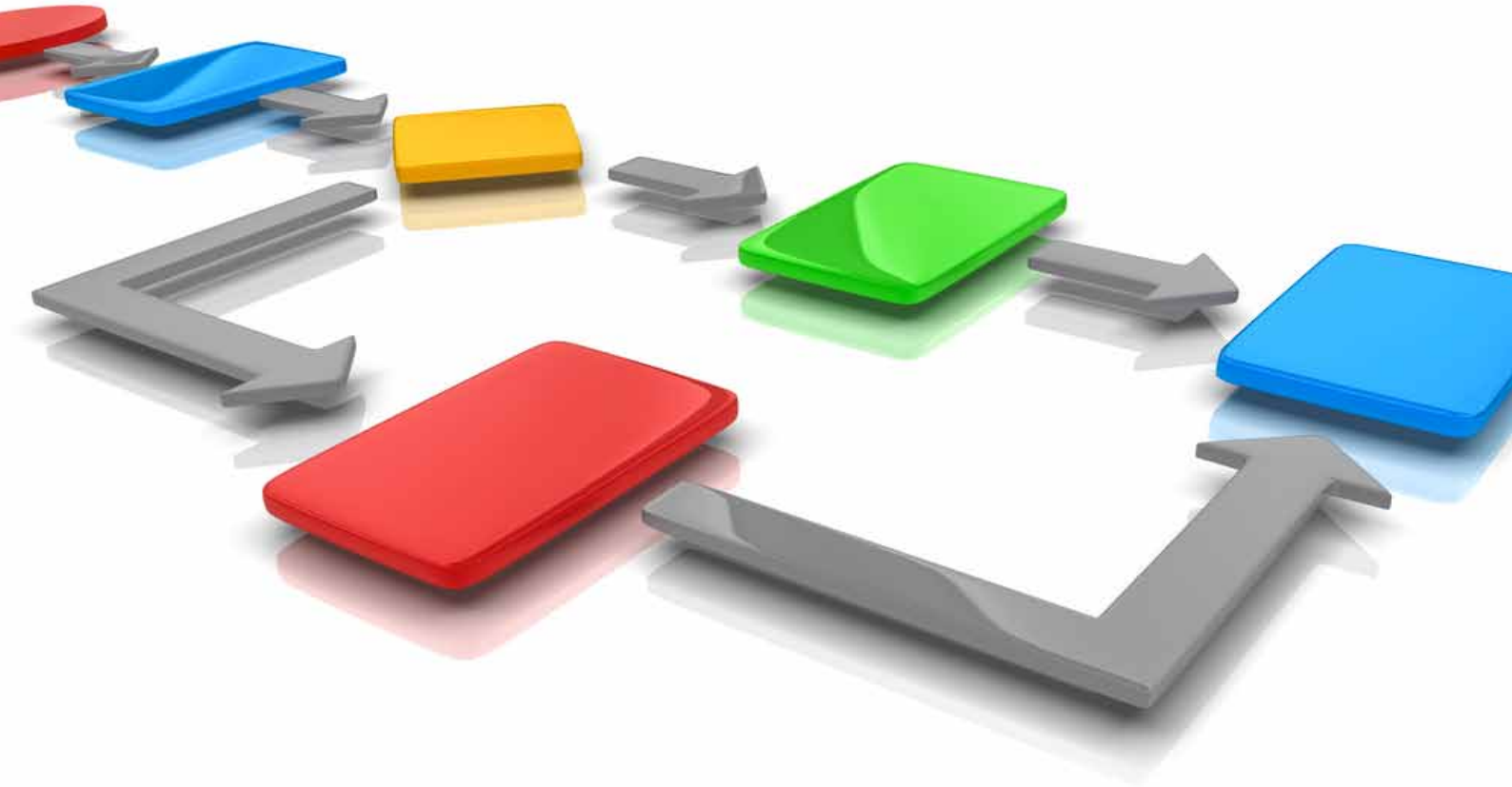
Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

# Over-the-Counter (OTC) Medicines Business Process Reform

## Consultation Paper

Version 1.0 September 2012



# About the Therapeutic Goods Administration (TGA)

- The TGA is a division of the Australian Government Department of Health and Ageing, and is responsible for regulating medicines and medical devices.
- TGA administers the *Therapeutic Goods Act* 1989 applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance), when necessary.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines and medical devices.
- The TGA relies on the public, healthcare professionals and industry to report problems with medicines or medical devices. TGA investigates reports received by it to determine any necessary regulatory action.
- To report a problem with a medicine or medical device, please see the information on the TGA website <www.tga.gov.au>.

# About Medsafe

- Medsafe is the New Zealand Medicines and Medical Devices Safety Authority and is responsible for the regulation of therapeutic products in New Zealand through administration of the *Medicines Act 1981*.
- Medsafe is a business unit of the New Zealand Ministry of Health.
- Medsafe's Mission is: 'To enhance the health of New Zealanders by regulating medicines and medical devices to maximise safety and benefit.'
- In working to achieve the stated mission Medsafe:
  - applies accepted international practice to the regulation of therapeutic products
  - provides efficient services measured against agreed stated performance indicators
  - prepares and maintains regulatory guidelines reflecting sound science and promoting evidence based decisions
  - applies processes that are consistent, transparent and minimise the costs of regulatory action
  - provides timely and unbiased information to health professionals and consumers about the safe use of therapeutic products.
- To find out more about medicines regulation in New Zealand please see the information on the Medsafe website at <www.medsafe.govt.nz>.

# Contents

# How to make a submission

You are invited to provide written comment on this consultation paper. Submissions can be sent by post or e-mail and, where possible, should be cross-referenced to the specific sections set out in this consultation paper.

# Content of submissions

## Your submission should include:

- your name and full contact details including: address, telephone number, email and if applicable facsimile
- the particular issue being addressed
- relevant evidence and/or examples to support the views expressed
- in the case of organisations, the level at which the submission was authorised.

**Please note**: Submissions should be confined to the specific subject matter of this consultation paper. Any submissions received that do not directly relate to the subject area, or that reference other consultation papers, will not be considered.

## Confidentiality of submissions

If you wish any information contained in your submission to be treated as confidential, please clearly identify that information and outline the reasons why you consider it to be confidential. Note that general disclaimers in covering emails will not be taken to be sufficient reason for submissions to be treated confidentially.

## Address for submissions

- Electronic submissions should be e-mailed to:

  Medsafe: medsafeapplications@medsafe.govt.nz

  TGA: OTCBPRconsultationpaper@tga.gov.au

  with OTC BPR in the subject heading.

- Hardcopy submissions should be mailed to one of the following addresses:

OTC Medicines Regulatory Process Review
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606
AUSTRALIA

Manager Product Regulation
Medsafe, Ministry of Health
PO Box 5013
WELLINGTON 6011
NEW ZEALAND

# Questions relating to submissions

## In Australia:

Any questions relating to submissions should be directed to the ***OTC Medicines Business Process Reform***, via email to **OTCBPRconsultationpaper@tga.gov.au**

## In New Zealand:

Any questions relating to submissions should be directed to the ***Manager Product Regulation***, via email to **medsafeapplications@medsafe.govt.nz**

# Deadline for submissions

The deadline for receipt of submissions is*:* **7 November 2012.**

# Next steps

Analysis of submissions is expected to be completed, final decisions made and the outcome notified on the Medsafe website at <http://www.medsafe.govt.nz> and the Therapeutic Goods Administration website at <http://www.tga.gov.au> by the end of 2012. Implementation of the changes is expected to commence in both countries by the end of April 2013.

# Introduction and overview

On 20 June 2011 the Prime Ministers of Australia and New Zealand reaffirmed their commitment to the establishment of the Australia New Zealand Therapeutic Products Agency (ANZTPA) and joint regulatory scheme. Details of the June 2011 announcement can be found at <http://www.pm.gov.au/press-office/landmark-agreement-achieve-world-standards-therapeutic-products> and at <http://www.beehive.govt.nz/release/australia-nz-announce-intention-anztpa>.

A three-phase staged approach to achieving the establishment of ANZTPA by 2016 has been adopted. As part of the first stage of this process, Medsafe and the TGA have commenced a programme of work-sharing and increased joint operations. The OTC Medicines Business Process Review (OTC BPR) project is one of the projects under this work programme.

The objective of the medicines legislation in both countries is to protect public health by managing the risk of avoidable harm associated with the use of medicines. The legislation specifies that before a medicine is approved for marketing it must be demonstrated that it meets applicable standards of safety, quality and efficacy. The legislation also provides Medsafe and TGA with powers to take appropriate action if evidence suggests that a medicine does not meet these standards at any time after it has been approved for marketing.

Both Medsafe and the TGA apply frameworks of controls designed to ensure that therapeutic products have greater benefits than risks if used appropriately, and achieve this through a continuous monitoring process that couples the pre-market approval requirements with post-market surveillance functions.

# Objectives and scope of the OTC Medicines Business Process Review project

TGA and Medsafe have been working with OTC medicines industry representatives on a review and reform of the business processes for the evaluation of over-the-counter (OTC) medicines. The objectives of the reforms are to:

- deliver more efficient and cost-effective OTC medicines evaluation processes
- provide greater transparency and predictability of the regulatory process
- ensure consumers have timely access to safe and effective OTC medicines
- harmonise the OTC medicines evaluation processes in Australia and New Zealand
- improve the quality of OTC medicine applications lodged with TGA and Medsafe
- ensure an appropriate benefit/risk model is applied to approvals of OTC medicines
- deliver appropriate cost recovery of OTC medicines regulation.

Proposed strategies for achieving these objectives are set out in this consultation paper. In summary, it is proposed to:

- establish risk categories for OTC medicines applications
- determine the characteristics of applications falling into each risk category
- define application requirements, business processes and target times for applications in each application risk category
- develop OTC medicine monographs (OMMs) for previously-approved and well-characterised active ingredients
- require applications to be in the common technical document (CTD) format

In addition, it is envisaged that implementation of the proposals in Australia would:

- provide sponsors with better information about the progress of their applications through the evaluation process
- improve publicly available information about the regulation of OTC medicines.

The following matters are outside the scope of this project and are not included in this consultation paper:

- Development and implementation of a process that enables lodgement of a single application for approval in both the Australian and New Zealand jurisdictions will only be achieved with the establishment of the joint scheme and is not discussed in this paper.
- Requirements for labelling and packaging of OTC medicines in Australia are currently the subject of a separate review. The reform of the OTC medicines business process proposed in this consultation document would not impact on the outcomes of that review.

# Phased implementation of the new business processes

Following completion of consultation and before implementing any changes to the OTC medicines business processes, the following will occur.

- Development of a number of forms and guidelines including:
  - application form(s) that clearly specify data requirements for each category of application
  - updates to regulatory guidelines (business rules, process details, data requirements, labelling requirements)
  - assistance tool(s) to assist sponsors to determine the appropriate application category
  - frequently asked questions (FAQs) for sponsors.
- Development of a Cost Recovery Impact Statement for Australia, including a public consultation on a revised OTC medicines fee structure.

The business processes for OTC medicines articulated in this document have been developed as a proposed harmonised approach to the future regulation of OTC medicines by ANZTPA under the joint regulatory scheme.

It is recognised that the operating environments of Medsafe and the TGA are constrained by the separate national frameworks for the regulation of therapeutic products that are set out in current legislation (the *Therapeutic Goods Act 1989* in Australia and the *Medicines Act 1981* in New Zealand).

This consultation paper proposes that each country will phase the implementation of a harmonised OTC medicines business process over the period leading up to the establishment of ANZTPA in 2016. It is anticipated that the processes will continue to be refined during this time. To this end, Medsafe and TGA will conduct a review of the revised OTC medicine evaluation processes after 12-18 months of operation. This will involve consultation with the OTC medicines industry and other relevant stakeholders.

# Risk based approach to regulating OTC medicines

Medsafe and TGA apply risk management principles described in the international risk management standard, ISO 31000:2009, to the regulation of therapeutic products. This standard was also used as the basis for the risk categorisation frameworks for OTC medicine applications proposed in this consultation paper.

Risks are rated in terms of the likelihood of an event occurring and the consequence if it were to occur. Consequence is the outcome of an event affecting objectives, whereas likelihood is the chance of something happening, whether defined, measured or determined objectively or subjectively, qualitatively or quantitatively, and described using general terms or mathematically (such as a probability or a frequency over a given time period).

Medsafe and the TGA have used the risk matrix shown in Figure 1 to define levels of risk associated with OTC medicines in order to categorise applications for new and changed medicines and apply different data requirements and timelines to different risk categories.

| LIKELIHOOD Probability of Occurring | CONSEQUENCE Risk to Patient Outcome | | | | |
|---|---|---|---|---|---|
| | Negligible | Low | Medium | High | Extreme |
| Almost Certain | | | | HIGH | |
| Likely | | | MODERATE | | |
| Possible | | LOW | | | |
| Unlikely | NEGLIGIBLE | | | | |
| Very Unlikely | | | | | |

**Figure 1: General framework for rating of risk**

# Risk categorisation framework for OTC medicine applications

It is proposed that there would be five risk categories (Category N1 to Category N5) for applications for new medicines, as shown in Figure 2.

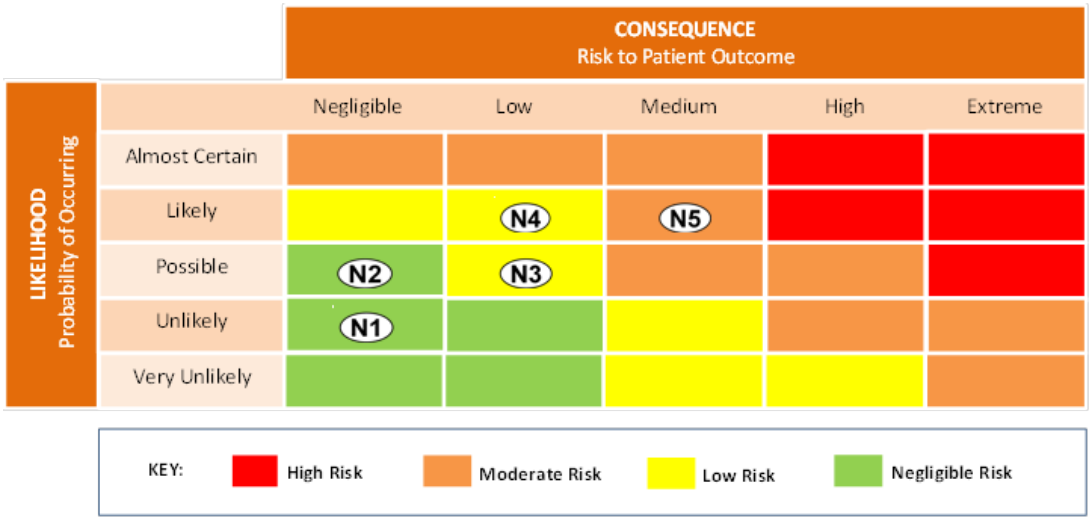



**Figure 2: Risk based application categories for new medicines**

It is proposed that there would be four risk categories (Category C1 to Category C4) for applications relating to changed medicines, as shown in the Figure 3.

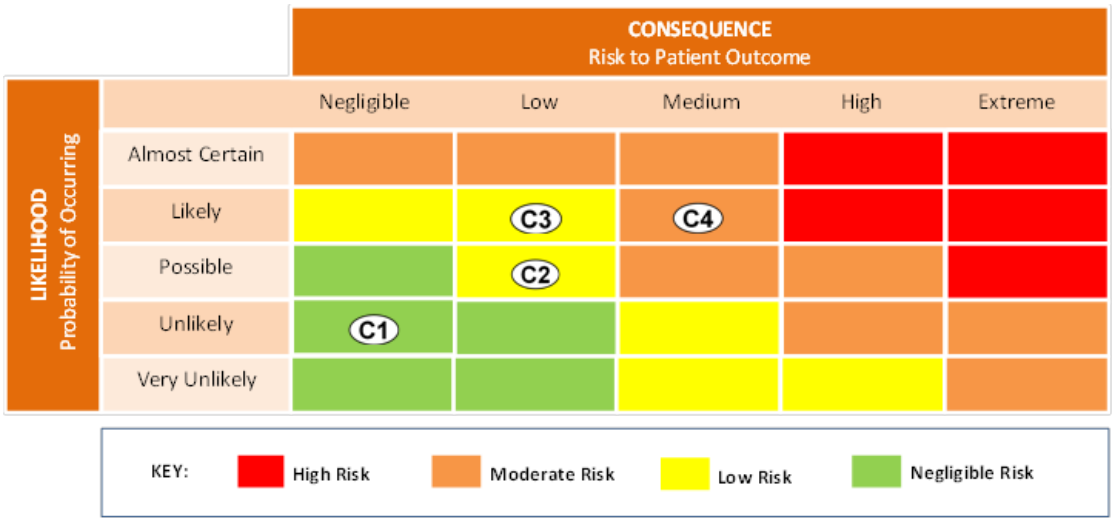



**Figure 3: Risk based application categories for changed medicines**

Each application category will have clearly defined submission requirements and timelines. OTC medicines containing well-understood active ingredients (such as aspirin and paracetamol) and clones of existing OTC medicines would fall into the lower risk categories, while more complex applications such as those involving new active ingredients or new indications would fall into the higher risk categories. Category 1 applications (N1 or C1) would require less supporting information and follow a shorter timeline than applications in higher categories (such as N5 or C4).

# New medicine applications

The proposed categories for new medicine applications and the criteria for inclusion in each category are summarised in Table 1 below. Further detail relating to each category is provided in Appendix 1.

**Table 1: Risk categorisation framework for new medicine applications**

| Risk rating | Application category | | Product/application criteria |
|---|---|---|---|
| Negligible | New medicines | N1 | Product is identical to an existing OTC product in all respects other than product name and/or classification statement<br>AND<br>Product name does not include an umbrella segment specified as requiring a higher level of assessment[1]. |
| | | N2 | Product complies with an OTC Medicine Monograph<br>AND<br>Product name does not include an umbrella segment specified as requiring a higher level of assessment [1].<br>AND<br>Product is not of a type specified in Note 1 to Appendix 1. |
| Low | | N3 | Product does not fall into category N1, N2 or N4<br>AND<br>Product does not comply with an OTC Medicine Monograph.<br>AND<br>Product name does not include an umbrella segment categorised as requiring a higher level of assessment[1]<br>AND<br>Product is not of a type specified in Note 1 to Appendix 1. |
| | | N4 | Product is of a type specified in Note 1 to Appendix 1<br>OR<br>Product name includes an umbrella segment categorised as requiring a higher level of assessment[1]<br>AND<br>Application does not meet the criteria for inclusion in Category N5. |

| Risk rating | Application category | | Product/application criteria |
|---|---|---|---|
| **Moderate** | **Extensions/NCE** | **N5** | Product contains a new chemical entity (NCE) as an active ingredient<br>OR<br>Product does not contain a new active ingredient but the application relates to :<br>· a new therapeutic indication<br>· a new strength<br>· a new dosage form<br>· new directions for use<br>· use in a different patient population<br>· a new combination product. |

[1] Refer to section on '*Application categorisation for umbrella branded medicines*'

## OTC Medicine Monographs (OMMs)

The risk categorisation framework shown in Table 1 describes the application risk categories for new medicine applications. The proposed framework includes a category (N2) for products that are comprised of well-characterised active ingredients, provided that the product complies fully with the applicable OTC Medicine Monograph (OMM). This category would have significantly reduced requirements for data assessment and consequently shorter evaluation timelines.

# Changed medicine applications

The proposed categories for applications for changes to approved OTC medicines are summarised in Table 2 below. Further detail relating to each category is provided in Appendices 2 and 3.

**Table 2: Risk categorisation framework for changed medicine applications**

| Risk rating | Application category | Type of change |
|---|---|---|
| **Negligible** | **C1** | ***Quality and Non-Quality Changes***<br>Minor non-quality and quality related changes |
| **Low** | **C2** | ***Quality Changes***<br>Changes to quality aspects of a product excluding changes described in levels C1 or C4[1].<br>***Non-Quality Changes*** - no safety & efficacy data required<br>Changes to the non-quality aspects of the product excluding changes described in C1, C3 or C4 and excluding changes requiring the provision of safety and efficacy data (or a justification for not providing such data)[1]. |
| | **C3** | ***a: Umbrella branding*** - higher level of assessment required<br>Changes to the product name where the new name includes an umbrella segment categorised as requiring a higher level of assessment[1]. |
| | | ***b: Non-Quality Changes*** -some safety & efficacy data may be required.<br>Changes requiring evaluation of safety and/or efficacy data to support changes to labelling (incl. PI or Data sheet / CMI) except those changes described in C4. |
| **Moderate** | **C4** | ***Non-Quality Changes*** – data required<br>Changes for which safety and efficacy data (clinical and/or toxicological) are required or where justification for not providing such data would be required. |

[1] Refer to section on '*Application categorisation for umbrella branded medicines*'

Due to legislative and operational requirements in Australia and New Zealand, implementation of the new processes for the following will not occur until the joint regulatory scheme commences. In New Zealand this will mean that:

- applications relating to some quality changes (new type of manufacturing process for a finished product, new manufacturing process for an active ingredient, new container/closure/ packaging, formulation changes, and new indications) will require full assessment and may be referred under section 24(5) of the Medicines Act 1981, and
- a change in product name where the product is replacing an existing product in the market will be assessed as a changed medicine application. A new medicine application will be required if the product is to remain available under both names.

## General questions on the proposed risk categorisation framework:

- Do you support the concept of risk-based categories for OTC medicines?
- Do you agree with the proposed risk categories for new medicines?
- Do you agree with the proposed risk categories for changed medicines?

# Proposed OTC medicines evaluation process

The business processes proposed in this document represent a harmonised approach to the regulation of OTC medicines in New Zealand and Australia. Full implementation of the proposed approach would require changes to the national legislative frameworks. Consequently, implementation of some aspects is not expected to occur until the joint regulatory scheme administered by ANZTPA comes into effect.

## Key features of the process

The proposed process is made up of five phases each with defined requirements for progressing to the next phase, as shown in figure 3. Each of these phases is explained in more detail below.

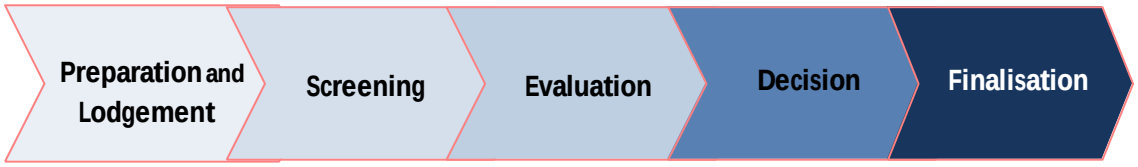



**Figure 3: Overview of proposed OTC medicines application process**

The following principles have been applied in developing the proposed process.

- Applications will be screened by the regulator upon receipt.
- Incomplete applications will not be accepted for evaluation and fees will be forfeited.
- There will be a maximum of two rounds of requests from the regulator for the applicant to supply additional information.
- Target timelines will be specified for the completion of each stage of the evaluation process.
- Target timelines will be specified for receipt of company responses to requests for additional information.
- The regulators will report actual time taken to complete stages in the evaluation process.
- Applicants will be able to monitor progress of applications through online access to a database maintained by the regulator.

## Preparation and lodgement phase

The process will commence when a sponsor makes an application seeking approval of new or changed medicines.

Medsafe and TGA will provide guidance materials to help sponsors identify the appropriate category for their application, which will in turn determine the information that the sponsor must supply.

The relevant supporting information will be required to be submitted electronically in CTD format. This will provide applicants with clarity about data requirements and enable the regulator to more easily locate specific elements of the data package.

## Application screening phase

Medsafe and the TGA will screen applications to check that the sponsor has correctly identified the application category and provided the required information for the application to proceed through to the next phase of the process. During screening the regulator will determine whether:

- the application category has been correctly identified
- the correct application fee has been paid
- all the required information has been provided.

Application Screening will have two parts. The first will be an administrative check to ensure that the administrative requirements of the application have been satisfied (e.g. payment of the application fee and completeness of contact details). The second will be a technical screen to determine the nature and complexity of the application and to determine whether the application can be processed further.

## Payment of fees

Fees will be payable upon receipt of an application. If an application is deficient it will not be accepted for evaluation and the application fee will be forfeited.

During the period prior to establishment of ANZTPA, payment of fees will be in accordance with current national requirements as indicated below.

*Australia*

In accordance with section 23(2)(a) of the *Therapeutic Goods Act 1989*, an application will be deemed to be not effective unless the prescribed application fee has been paid. The current process where sponsors generate their own invoices and make arrangements for payment of the fees at the time of lodgement will continue.

Once payment has been confirmed as correct for the application type, the TGA will confirm payment by issuing a receipt for the payment which will be sent to the sponsor. The receipt signifies that the application has been received by the regulator and has entered the screening phase. The application screening will result in an administrative decision that the application is effective or not effective under section 23(2)(b) of the *Therapeutic Goods Act 1989*.

Where an application is deemed to be ineffective, the sponsor will be notified and provided with a list of deficiencies.

If the application is considered complete, the sponsor will be advised that the application will be accepted, and an evaluation invoice generated.

*New Zealand*

Applications will be screened upon receipt. If the application meets all the relevant requirements an invoice will be issued. Upon payment of the invoice the application will proceed to the evaluation phase.

# Evaluation and review phase

The evaluation and review phase involves:

- Allocating resourcing to the application evaluation.
- Evaluation of the information provided by the sponsor in accordance with the requirements of the applicable application category.
- Up to two requests for information (RFI) to clarify specific aspects of the application.
- Documentation of findings and a recommendation for approval or rejection.

This phase is shown in greater detail in the diagram below.

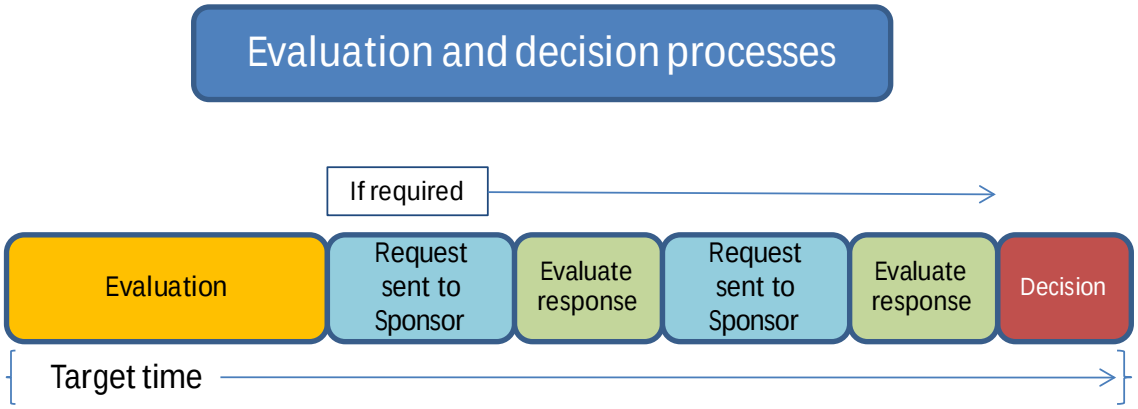



**Figure 4: Proposed OTC medicine evaluation and decision process**

The evaluation and review phase allows the regulator to seek clarification about any component of the application that affects the safety, quality or efficacy of the product and the risks and benefits to consumers. In cases where clarification is needed, a consolidated set of questions will be prepared by the regulator and sent to the sponsor as a RFI letter. There may be up to two requests for information to clarify specific aspects of the application.

The RFI will include sufficient information to allow the sponsor to understand the issues and concerns. It will also specify the maximum number of days allowed for the sponsor to provide a formal response. Prior to the establishment of ANZTPA, Medsafe will specify a fixed number of days, whereas the TGA will allocate a reasonable period of time on a case-by-case basis and formally notify the sponsor.

The sponsor's response will need to address all issues raised, and if a response is not received within the specified timeline or only a partial response is received, the evaluation and decision making process may proceed on the basis of the information available.

It should be noted that once evaluation has commenced, the sponsor will not be able to make changes to the application or submit additional information. The RFI process is not intended to provide sponsors with an opportunity to supply information that should have been included in the original application.

The regulator will conclude the assessment by considering the safety, quality and efficacy of the proposed OTC medicine. The benefits and risks of the medicine will be assessed and documented in the evaluation report, which will contain a recommendation on whether to approve or reject the application.

When necessary, advice on specific issues relating to the application may be sought from an appropriate advisory committee which has expertise in the safety, quality and efficacy of OTC medicines (the ACNM in Australia or the MAAC in New Zealand). Historically, in Australia, this occurs for 3% to 4% of applications. Where an application is referred to an advisory committee for advice, application processing timelines will be adjusted accordingly.

## Decision phase

Under the joint regulatory scheme there will be a single decision-making process with effect in both countries. However, until ANZTPA is established, the decision-making processes will continue to occur as currently specified in Australian or New Zealand legislation.

### General questions on the proposed OTC medicines evaluation process:

- Do you support the proposed five-phase process?
- Do you agree with the principles that were applied when developing the proposed process?

# OTC medicine monographs

It is proposed that OTC medicine monographs (OMMs) will be developed for OTC medicines containing well-characterised active ingredients. The monographs will specify requirements in relation to:

- active ingredients, dosage forms and strengths
- indications and claims
- directions for use
- labelling and advisory statements
- quality standards.

Good regulatory practice principles require that the proposed monographs draw on international standards and existing regulatory controls, except in circumstances where there is a clear public health need to introduce and explicitly clarify additional controls.

Where a proposed new medicine complies with all the requirements specified in the applicable monograph, the application would fall under the new medicine application category N2, allowing the sponsor to submit an abbreviated data package. However, a full data package must be held by the sponsor.

All relevant requirements under the *Therapeutic Goods Act 1989* and the *Medicines Act 1981* will continue to apply to OTC medicines, including those medicines that are covered by an OTC medicine monograph.

Sponsors will be required to provide written assurances that the medicine meets all the requirements of the OMM. Post-market monitoring of compliance with all requirements will be conducted and appropriate enforcement action taken where non-compliance is detected.

Medsafe and TGA will consider developing an OTC medicine monograph for OTC medicines for which:

- there is a high level of knowledge and experience within Medsafe and the TGA with the active ingredient(s) in the medicine
- evaluation of bioavailability, bioequivalence or other clinical data is not required
- a relevant British Pharmacopoeia/US Pharmacopoeia product monograph exists
- the quality aspects can be sufficiently assured through sponsor assessment and assurance.

OTC medicine monograph development will be initiated and undertaken by Medsafe and the TGA. Priority will be given to active ingredients where the expected frequency of applications is sufficient to justify the resources involved in developing the monograph.

It is proposed that the following OTC medicine monographs will be developed prior to the implementation of the new medicine application business process:

- Paracetamol
- Aspirin
- Ibuprofen
- Topical antifungals such as clotrimazole and miconazole
- Paracetamol/codeine combination
- Ranitidine hydrochloride.

These active ingredients were selected as priority targets based on analysis of recent Australian applications. It is anticipated that over time the list of OTC medicine monographs will expand to cover other medicines.

OTC medicine monographs will require review and updating in order to reflect current knowledge and standards and in response to concerns that may arise. Reviews will be undertaken by Medsafe and the TGA.

## General questions about the proposal to develop monographs:

- Do you support the concept of developing monographs for some OTC medicines?
- Do you agree with the proposed list of medicines that should be given priority for monograph development?

# Application categorisation for umbrella branded medicines

Determination of the application category for an umbrella branded product should be made using the criteria set out in the risk categorisation frameworks (see appendices 1 and 2) and in conjunction with the additional information detailed below.

## What is umbrella branding?

**'Umbrella branding'** refers to the marketing of two or more medicines under the same proprietary 'brand' name. This is sometimes referred to as 'brand name extension' or 'trade name extension'.

The **'umbrella segment'** is the part of a medicine name that is used in the name of more than one medicine to create a 'brand' for a range of medicines.

The use of umbrella branding in OTC medicines is generally associated with:

- particular active ingredients
- a therapeutic area or set of indications
- a particular sponsor or retailer.

**'House brand'** is a term used to describe a range of medicines where the umbrella segment of the medicine's name is typically associated only with the sponsor or retailer. These ranges of medicines are not associated with any particular active ingredient(s), or therapeutic area and indications(s), and usually the 'house brand' spans a wide range of unrelated medicines.

## Possible risks associated with umbrella branding

The presentation of any new medicine, including its trade name, must be clear, unambiguous, not misleading in any way with regard to the nature, purpose, uses or effects of the product, and not easily confused with any other product registered for use.

In certain circumstances the use of umbrella branding may result in several look-alike and sound-alike medicines available for self-selection. Consumers may not be aware of important differences or similarities between these medicines.

Examples of umbrella branding are the extension of a trade name to include a new medicine with one or more different active ingredient(s) and/or a new medicine that is for the treatment of a condition not previously covered by the trade name.

The majority of OTC medicines in umbrella branded ranges, such as 'house brands', do not pose safety or efficacy concerns. However, there may be situations where the proposed name of a new medicine increases the risk of self-medication errors. In these circumstances the risk categorisation of the application will change as described below.

Medsafe and the TGA will continue to assess the acceptability of applications that involve an extension to an umbrella brand against the guidance outlined in the relevant sections of the ARGOM and the NZRGM. These guidelines should be referenced by all sponsors prior to submitting a new or changed medicine application for an OTC medicine in either Australia or New Zealand.

## Risk categorisation framework

Within the proposed risk categorisation frameworks, applications for umbrella brand extensions are identified as requiring an increased level of assessment when the risks to consumers are considered to be higher. These applications are classified as category N4 or N5 for new medicines and category C3 or C4 for changed medicines. Medsafe and the TGA will

develop guidelines, based on the following approach, to assist sponsors to determine the correct application risk category for applications relating to an umbrella branded medicine.

## Negligible to low risk associated with the use of the umbrella segment.

Applications in which the umbrella segment is considered to pose a negligible to low risk to consumers can usually be managed by ensuring adequate differentiation across the range. Consequently, the categorisation of these applications is not affected by the umbrella branding and sponsors should determine the application category based on other criteria.

Applications that usually fall within this category include applications involving a medicine that is:

- within a house brand, or
- a different strength or dosage form but has the same active ingredient(s) as previously approved for medicines within the umbrella brand.

## Higher risk associated with the use of the umbrella segment.

Applications that propose an extension of an umbrella brand involving an active ingredient, combination of active ingredients, or indications that have not previously been included under that umbrella brand are considered likely to pose an increased safety and/or efficacy risk to consumers.

For these types of applications, the suitability of the umbrella segment in the medicine name requires a higher level of assessment in order to manage the relevant risks to consumers.

Such applications will be in category N4 or N5 for new medicines, or category C3 or C4 for changed medicines, depending on other characteristics of the product or product changes.

# Target times

To provide sponsors with predictable timelines, Medsafe and TGA are currently using historical data to forecast the percentage of applications that will go through each application category and to determine realistic target timelines. It is important to note, however, that Medsafe and TGA can commit to meeting target timelines only where the sponsor has provided a complete and quality application.

Target timelines will be expressed in calendar days and will exclude time taken for sponsors to respond to questions. The initial performance indicator proposed is for completion of 80% of applications in each category within target timelines. A post-implementation review will assess the effectiveness of the timelines and performance indicators after 12-18 months of operation.

Based on estimates from historic data, the timelines currently achieved by Medsafe and the TGA are significantly different. As one of the aims of this business process review is to deliver more efficient and cost-effective OTC medicines processes, the target timelines proposed for the joint regulatory scheme are shorter than those currently achieved by either regulator. Figures 5 and 6 below show the aspirational timelines for ANZTPA in 2016.

## Aspirational timelines to be achieved by the establishment of ANZTPA in 2016

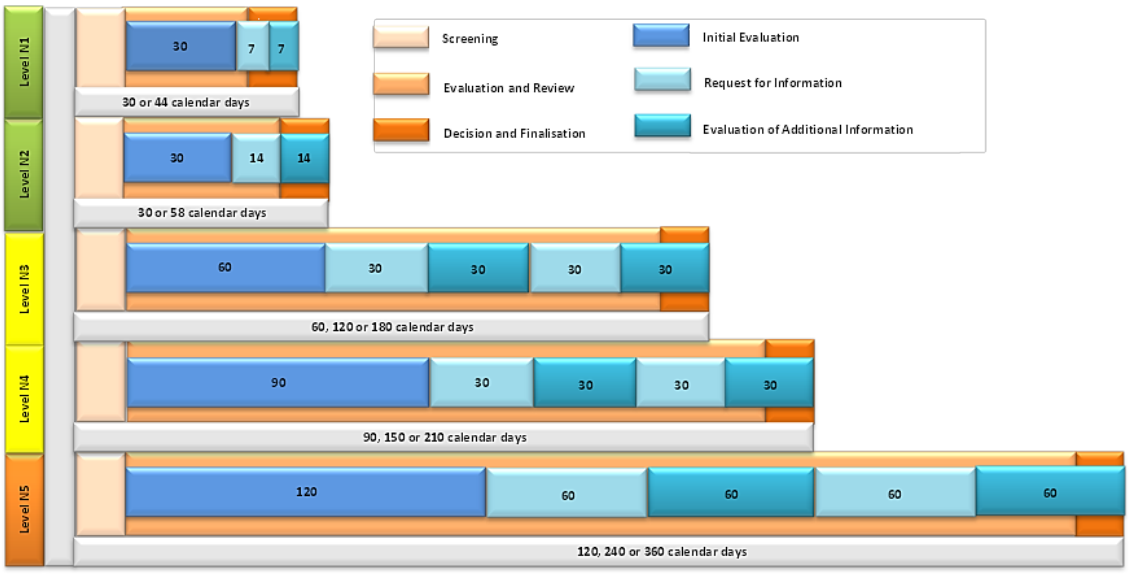



**Figure 5: Aspirational timelines for new medicine applications**

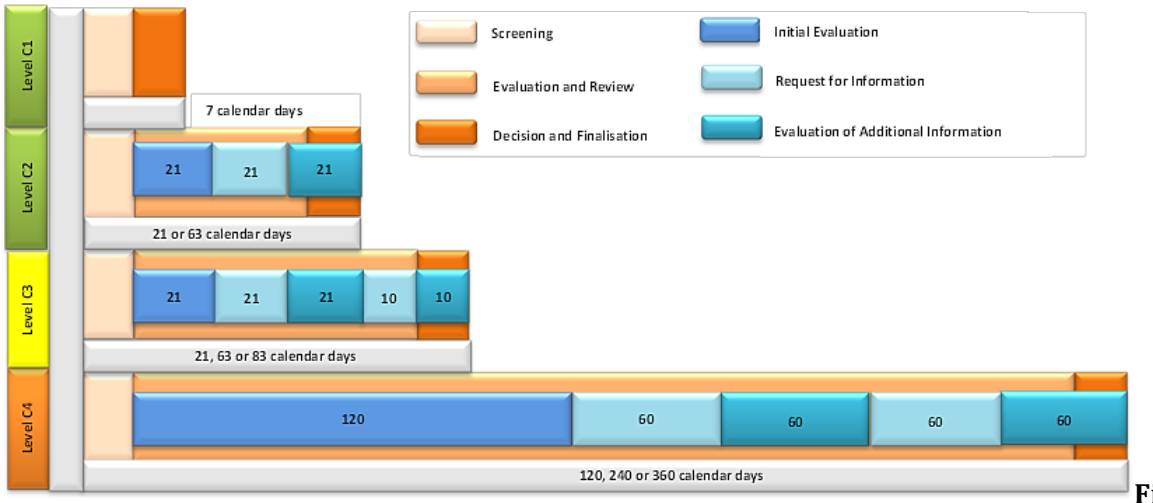



**Figure 6: Aspirational timelines for changed medicine applications**

Medsafe and the TGA will each progressively move towards the targets from their respective starting points, and will publish performance at appropriate (e.g., 6 monthly) intervals between the implementation of the revised OTC medicine processes and the establishment of ANZTPA in 2016.

It should be recognised that in order to achieve this level of activity cultural and operational changes will be required within both Medsafe and the TGA.

# Medsafe target timelines for the revised OTC medicine evaluation process

In New Zealand it is intended that, within three months of implementing the revised business process, Medsafe will achieve the aspirational timelines for ANZTPA.

# TGA target timelines for the revised OTC medicine evaluation process

Figure 7 shows the proposed target timelines that TGA will initially implement. These targets represent a significant reduction in current timelines. In the case of complex applications the proposed timelines represent a reduction of 13% to 30% of the timelines achieved in 2011.

However, it is important to note that the TGA currently has a backlog of OTC medicine applications. Although efforts are being made to reduce this backlog, the TGA's ability to achieve the target timelines and performance indicators depends on the size of the backlog at the commencement of the new process.

Later in 2013 the TGA will be releasing a consultation paper on the proposed revision to the OTC fee framework. The TGA is currently conducting a detailed investigation of process stages and timelines that will further define the targets for individual phases of the evaluation process.

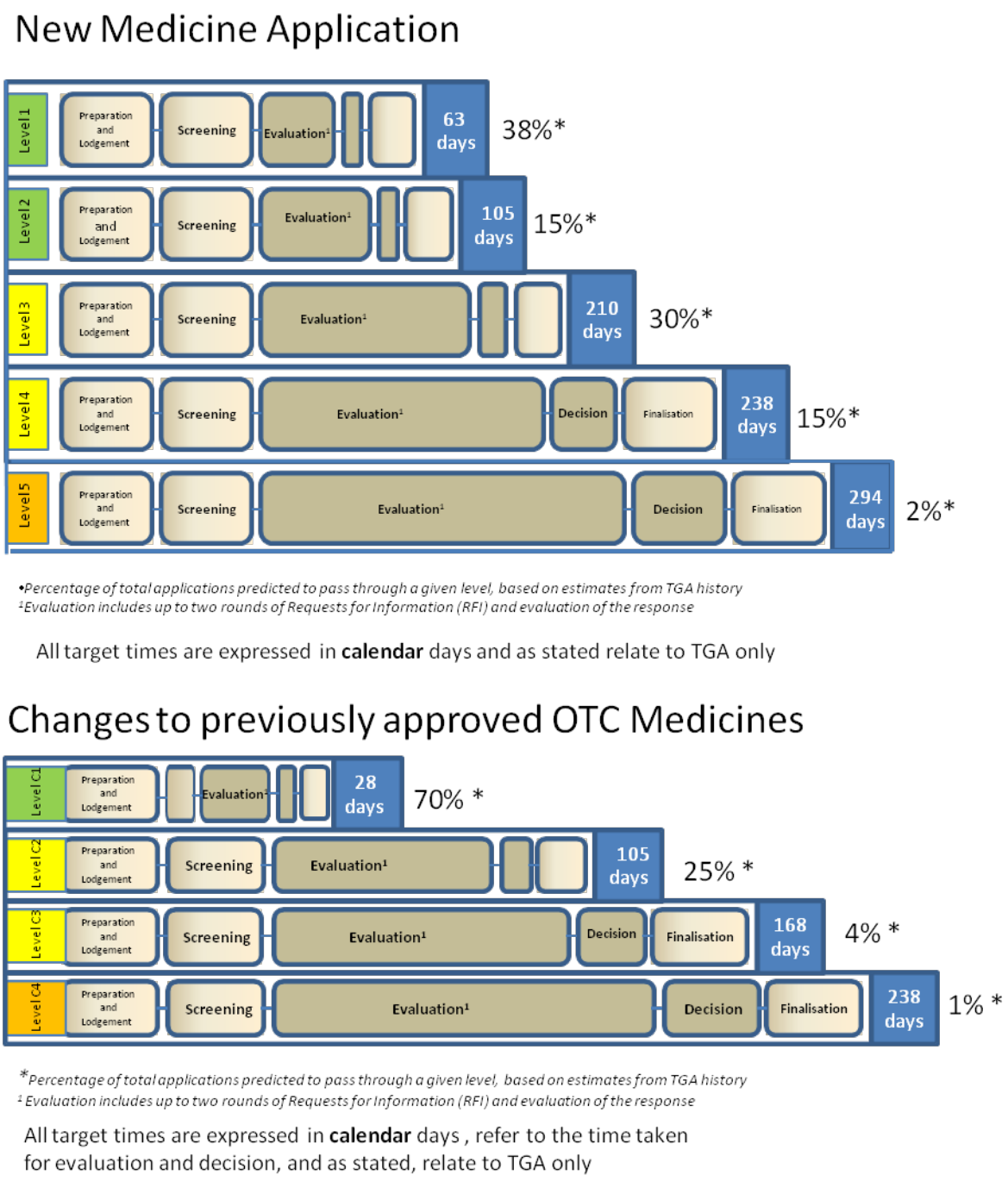



**Figure 7: First stage target timelines for the TGA**

# Appendices

1. Risk categorisation framework for new medicine applications (including definitions of each category and data requirements)
2. Risk categorisation framework for changed medicine applications (including definitions of each category and data requirements)
3. Changes tables (Medsafe and TGA)
4. OTC BPR Glossary

## Appendix 1: Risk categorisation framework for new medicine applications:

| Risk Rating | Application Category | | Product/application criteria | Explanatory Notes | CTD module | Information requirements |
|---|---|---|---|---|---|---|
| **Negligible** | **New medicines** | **N1** | · Product is identical to parent product other than product name, and/or classification statement<br>· Product name does not include an umbrella segment categorised as requiring a higher level of assessment[1] | · Parent product must have been fully evaluated (safety, efficacy and quality)<br>· Full access to the rights of the product must be provided<br>· Evaluation includes compliance with RASML and/or Medsafe Labelling Statements Database | Module 1<br><br>Module 3 | Application / Assurances / Letter of authorisation / Evidence of GMP / Labels (PI/Data sheet and CMI as required)<br><br>Finished Product Specification (FPS) |
| | | **N2** | · Product complies fully with an OTC Medicine Monograph<br>· Product is not of a type specified in Note 1 to this Appendix<br>· Product name does not include an umbrella segment specified as requiring a higher level of | · Supporting information to demonstrate compliance with OTC Medicine Monograph | Module 1<br><br>Module 3 | Application / Assurances / Evidence of GMP / Labels (PI/Data sheet and CMI as required)<br><br>FPS and Certificates of Analysis (minimum of two) |

| Risk Rating | Application Category | | Product/application criteria | Explanatory Notes | CTD module | Information requirements |
|---|---|---|---|---|---|---|
| | | | assessment [1] | | | |
| Low | | N3 | · Product does not fall into categories N1, N2 or N4<br>· Product does not comply with an OTC Medicine Monograph<br>· Product is not of a type specified in Note 1 to this Appendix<br>· Product name does not include an umbrella segment categorised as requiring a higher level of assessment [1] | · Quality data to be evaluated<br>· Does not entail evaluation of safety and efficacy data as data previously evaluated and approved for other medicines<br>· No safety and efficacy data provided | Module 1<br><br>Module 3 | Application / Assurances / Evidence of GMP / Labels (PI/Data sheet and CMI as required)<br><br>Complete Module[2] (except where ARGOM / NZRGM specifies that a complete module is not required) |
| | | N4 | · Product is of a type specified in Note 1 to this Appendix<br>or<br>· Product name includes an umbrella segment categorised as requiring a higher level of assessment[1]<br>and<br>· Product/application does not meet the criteria for inclusion in N5 | · Quality data to be evaluated<br>· Safety and/or efficacy data (supporting clinical and/or toxicological data) provided or justification for not providing the data | Module 1<br><br>Module 2<br><br>Module 3<br><br>Module 4<br><br>Module 5 | Application / Assurances / Evidence of GMP / Labels (PI/Data sheet and CMI as required)<br><br>As applicable[2]<br><br>Complete Module[2] (except where ARGOM / NZRGM specifies that a complete module is not required)<br><br>As applicable[2]<br><br>As applicable[2] |

| Risk Rating | Application Category | | Product/application criteria | Explanatory Notes | CTD module | Information requirements |
|---|---|---|---|---|---|---|
| **Moderate** | **Extensions / NCE** | **N5** | · Product contains a new chemical entity as an active ingredient<br>or<br>· Product does not contain a new active ingredient but the application relates to:<br>– a new therapeutic indications<br>– a new strengths<br>– a new dosage form<br>– new directions for use<br>– new combination products<br>– use in a different patient population | · Quality data to be evaluated<br>· Safety and/or efficacy data (supporting clinical and/or toxicological data) provided or justification for not providing the data | Module 1<br>Module 2<br>Module 3<br>Module 4<br>Module 5 | Application / Assurances / Evidence of GMP / Labels (PI/Data sheet and CMI as required)<br>Complete Module<br>Complete Module[2] (except where ARGOM / NZRGM specifies that a complete module is not required)<br>As applicable[2]<br>As applicable[2] |

[1] Refer to section on 'Application categorisation for umbrella branded medicines'

[2] CTD Module requirements for OTC to be fully explained at a later date in a revised ARGOM/NZRGM

## Note 1

· Modified release products (excluding enteric coated tablets/capsules)

· Application for a generic of a registered product where bioequivalence data are required or where a justification for not providing bioequivalence is required

· Product includes a new excipient or an excipient with a new route of administration

- Applications for products where a PBS brand equivalence statement is requested and where bioequivalence evaluation is required or where a justification for not providing bioequivalence is required
- Formulation dependent topical products
- An application for an OTC product as a result of a change in scheduling for the particular product from the 'Prescription Only Medicine' schedule to a lower (OTC) schedule, where no such products are previously approved as an OTC medicine

# Appendix 2: Risk categorisation framework for changed medicine applications:

The identification of the broad categories is based on the impact or effect the proposed change will have on an approved medicine.

NOTE: Where a change application includes multiple changes covering different categories, the whole application is to be classified at the level of the highest category change in the application.

| Risk Rating | Application Category | Type of Change | Criteria | Explanatory Notes | CTD Module | Information Requirements |
|---|---|---|---|---|---|---|
| **Negligible** | **C1** | ***Quality and Non-Quality Changes***<br>· Includes minor non-quality and quality related changes | Changes specified in Table 1 (see Appendix 3) | This category would be equivalent to the types of changes previously categorised as an 'N' (notification) in ARGOM Ch.11 and as a 'Self-Assessable' change in the NZRGM | Module 1<br><br>Module 3 | Application / Assurances / Evidence of GMP(where required) / Labels(PI/Data sheet and CMI as required)<br><br>As applicable[2] |
| **Low** | **C2** | ***Quality Changes***<br>· Changes to quality aspects of a product excluding changes described in levels C1 or C4 | Changes specified in Table 2 (see Appendix 3) | Includes changes to product name except those changes involving an umbrella branded product where the umbrella segment is categorised as requiring a higher level of assessment[1] – assessed in level C3 | Module 1 | Application / Assurances / Evidence of GMP(where required) / Labels(PI/Data sheet and CMI as required) |

| Risk Rating | Application Category | Type of Change | Criteria | Explanatory Notes | CTD Module | Information Requirements |
|---|---|---|---|---|---|---|
| | | ***Non-Quality Changes*** - no safety & efficacy data required<br>Changes to the non-quality aspects of the product excluding changes described in C1, C3 or C4 and excluding changes requiring the provision of safety and efficacy data (or a justification for not providing such data)[1] | | This category can include changes to a product involving a new indication or directions for use /new patient population but only where the provision of safety & efficacy data are not required. For example, a new indication for a registered product where that indication has been previously approved for a very similar ('generic') product. | Module 3 | As applicable[2] |
| | **C3** | ***a: Umbrella branding: higher level of assessment***<br>· Changes to the product name where the new name includes an umbrella segment categorised as requiring a higher level of assessment[1] | Changes specified in Table 3 (see Appendix 3) | Changes to the product name where the new name includes an umbrella segment categorised as requiring a higher level of assessment[1]. | Module 1<br>Module 2<br>Module 3<br>Module 4 | Application / Assurances / Evidence of GMP(where required) / Labels(PI/Data sheet and CMI as required)<br>As applicable[2]<br>As applicable[2, 3]<br>As applicable[2] |

| Risk Rating | Application Category | Type of Change | Criteria | Explanatory Notes | CTD Module | Information Requirements |
|---|---|---|---|---|---|---|
| | | ***b: Non-Quality Changes*** -some safety & efficacy data may be required<br>· Changes requiring evaluation of safety and/or efficacy data to support changes to labelling (incl. PI or Data sheet / CMI) except those changes described in C4 | | Changes requiring evaluation of safety and/or efficacy data other than a new indication or directions for use / new patient population | Module 5 | As applicable[2] |
| **Moderate** | **C4** | ***Non-Quality Changes*** – data are required<br>· Where safety and efficacy data (clinical and/or toxicological) are required to support the proposed changes or where a justification for not providing such data would be required | Changes specified in Table 4 (see Appendix 3) | This category includes changes to a product's indications or directions for use (or the inclusion of a new patient population) where the provision of safety and/or efficacy data are required or a justification for not providing data is required | Module 1<br>Module 2<br>Module 3<br>Module 4<br>Module 5 | Application / Assurances / Evidence of GMP(where required) / Labels(PI/Data sheet and CMI as required)<br>Complete Module<br>As applicable[2, 3]<br>As applicable[2]<br>As applicable[2] |

[1] Refer to section on '*Application categorisation for umbrella branded medicines*'

[2] CTD Module requirements for OTC fully explained in a revised ARGOM / NZRGM

[3] Relevant only if application also includes Quality changes

**It should be noted that implementation of the risk frameworks under current New Zealand legislation will require that:**

1. Some quality changes will continue to require full assessment and may be referred under section 24(5) of the *Medicines Act 1981*. These changes include 'New type of manufacturing process for a finished product', 'New manufacturing process for an active ingredient', 'New container/closure/packaging', 'Formulation changes' and 'New indications'.
2. A change in product name where the re-named product is replacing an existing product in the market will be assessed as a change application, whereas a new medicine application will be required if the product is to remain available under both names.

*The risk categorisation framework for changed medicines has been amended to remove the 'Non-approvable changes" category (category V1). This class of change to a medicine will remain available to Australian sponsors (as described in ARGOM Ch. 11 - change category 'O'), but will not be included in the risk categorisation framework as this model is only associated with applications lodged with the TGA and / or Medsafe. The word 'variation' (as used throughout the model) has also been amended to 'change' with consequent changes to the application categories i.e. now referred to as C1, C2, and C3 & C4.*

*The risk categorisation framework for changed medicines also includes reference to Tables 1-4 in the 'Criteria' column. These tables will be specific to Australia and New Zealand. A first draft of each of the four Australian and New Zealand changes tables has been attached in appendix 3; the information included in the Australian and New Zealand tables has been sourced from the "Changes Table" (ARGOM [2003] Ch.11) and "Changed Medicine Notification Form A" respectively and therefore reflects current practice in terms of data requirements. These changes tables are intended to assist in the selection of the correct change once the appropriate application category has been selected.*

# Appendix 3: Changes tables

## TGA changes table 1

Change types applicable for changed medicine applications lodged in Australia under application category C1

| Type of change | Change | Change code | Relevant section of the TG Act |
|---|---|---|---|
| Label changes | Therapeutic indications – removal of sub-set of indications from label | LIS | 9D(2) / 9D(3) |
| | Recommended storage conditions – more restrictive | PSC | 9D(3) |
| | Addition of more restrictive safety-related statements | LSR | 9D(2) |
| | Changes on label (signal headings, warning statements) in compliance with new SUSDP requirements, other than LSF | LSU | 9D(2) / 9D(3) |
| | Changes to bring a label into compliance with the Labelling Order – other than changes to the proprietary name, indications or directions for use | LLO | 9D(2) / 9D(3) |
| | Addition of a required representation to a label (Part 2 of Schedule 2 to the *Therapeutic Goods Regulations*) | LLR | 9D(2) |
| | Colour, font, type size only (no change in label copy) | LCF | 9D(3) |
| | Reformatting of pre-existing text (i.e. moving of blocks of text and not rewording – see LIW, LRT) | LFO | 9D(3) |
| Sponsor changes | Sponsor name/logo(same sponsor of goods) and/or change to manufacturer/supplier details on label | SSP | 9D(3) |
| | Transfer goods to another sponsor | STR | 9D(3) |

| Type of change | Change | Change code | Relevant section of the TG Act |
|---|---|---|---|
| Product detail changes | Pack size – other than liquids/semi-solids (see PLS) or metered dose aerosols (see PMZ) (see also KBT, KGL, KBL and KOT) | PSZ | 9D(3) |
| | Pack size – liquids/semi-solids | PLS | 9D(3) |
| | Visual identification | PVI | 9D(3) |
| | Shelf life – decrease | PSR | 9D(3) |
| | Shelf life – increase (in accordance with an approved stability testing protocol for that product) | PSP | 9D(3) |
| | Recommended storage conditions – more restrictive | PSC | 9D(3) |
| Formulation changes – active ingredient | Overage – decrease | AOV | 9D(3) |
| Formulation changes – excipient | Removal of fragrance, flavour, printing ink and/or colouring agent(s) if the total agent(s) are present at not more than 2% w/w or w/v (if grouping applies)<br>Note: This change may result in consequential changes (e.g. deletion from the label of declared ingredients that are no longer relevant; change to visual identification and finished product specifications) which should also be addressed in accordance with the 'Changes Table'. | ERT | 23 |
| | Type of starch | EST | 9D(3) |
| | Change to ingredients within a proprietary ingredient which is a flavour, fragrance, printing ink or colour (proprietary ingredient has same name) | EWI | 9D(3) |

| Type of change | Change | Change code | Relevant section of the TG Act |
|---|---|---|---|
| Packaging changes | Container material – if the container is a bottle, the goods are a solid dosage form (e.g. tablet) and the change is of a type listed in assurance 15 | KBT | 9D(3) |
| | Container material – if the container is a blister pack, the goods are a solid dosage form (e.g. tablet) and the change is of a type listed in assurance 18 | KBL | 9D(3) |
| | Closure | KCL | 9D(3) |
| | Introduction of a measuring device (e.g. spoon, cylinder) or applicator (e.g. finger cot) | KSP | 9D(3) |
| | Changes to existing measuring device (e.g. spoon, cylinder) or applicator supplied with the goods or removal of a measuring device or applicator, where other means of accurately measuring or applying the dose are readily available | KMD | 9D(3) |
| | Introduction of a primary pack (no new text or graphics) | KPA | 9D(3) |
| | Removal of a primary pack | KPX | 9D(3) |
| | Removal of refill pack | KRR | 9D(3) |
| Manufacturing changes – finished product | TGA licensed Australian manufacturer (includes site of manufacture) | MMA | 9D(3) |
| | Overseas manufacturer (includes site of manufacture), if GMP pre-clearance certificate provided | MOS | 9D(3) |
| | Manufacturing process (other than MBS) | MPR | 9D(3) |
| Product information | Addition of more restrictive safety-related statements | DRS | 9D(2) |

| Type of change | Change | Change code | Relevant section of the TG Act |
|---|---|---|---|
| Other | Correction of ARTG record in accordance with section 9D(1) of the *Therapeutic Goods Act 1989* | CTA | 9D(1) |

## TGA changes table 2

Change types applicable for changed medicine applications lodged in Australia under application category C2

| Type of change | Change | Change code | Change code also in another Changes Table* | Relevant section of the TG Act |
|---|---|---|---|---|
| Label changes | Proprietary name (if grouping applies) | GPN | C3 | 23 |
| | New therapeutic indications (if grouping applies) | GIN | C3 & C4 | 23 |
| | Therapeutic indications or directions for use – change of wording without altering meaning | LIW | | 9D(3) |
| | Therapeutic indications – addition of registered indications to label | LIR | | 9D(3) |
| | Directions for use – e.g. dosage instructions (if grouping applies) (See also LIW) | GDU | C3 & C4 | 23 |
| | Recommended storage conditions – less restrictive | PST | | 9D(3) |
| | Changes on label (signal headings, warning statements) in compliance with new SUSDP requirements, where the change in scheduling is from 'Prescription Only Medicine' (Schedule 4) to a lower schedule | LSF | C3 | 9D(2) / 9D(3) |
| | Introduction of new graphics/icons (other than as specified in change SSP) | LGR | | 9D(3) |
| | Rewording of pre-existing text without altering meaning (other than indications or directions for use – see LIW) | LRT | | 9D(3) |

| Type of change | Change | Change code | Change code also in another Changes Table* | Relevant section of the TG Act |
|---|---|---|---|---|
| | Deletion or addition of text to the label (e.g. addition or removal of claims such as *clinically proven, fast/rapid action*; general claims regarding the product, its nature, mechanism of action, qualifying statements, etc.) | LDT | C3 | 9D(3) |
| Product detail changes | Proprietary name (if grouping applies) | GPN | C3 | 23 |
| | Pack size – metered dose aerosols | PMZ | | 9D(3) |
| | New therapeutic indications (if grouping applies) | GIN | C3 & C4 | 23 |
| | Shelf life – increase (other than in change PSP) | PSL | | 9D(3) |
| | Approval of a stability testing protocol for a specific product | PPR | | 9D(3) |
| | Recommended storage conditions – less restrictive | PST | | 9D(3) |
| | Sterility status/technique | PMI | | 9D(3) |
| Formulation changes – active ingredient | Overage – increase | AOA | | 9D(3) |
| | Change to amount of an excipient ingredient within a proprietary ingredient which contains an active substance (e.g. a direct-compression paracetamol mix) (if grouping applies) | GPA | | 23 |
| Formulation changes – excipient | Removal and/or addition of a fragrance, flavour, printing ink or colouring agent (if grouping applies), other than change ERT | GPI | | 23 |
| | Amount of excipient (if grouping applies) | GEX | | 23 |

| Type of change | Change | Change code | Change code also in another Changes Table* | Relevant section of the TG Act |
|---|---|---|---|---|
| | Change to ingredients within a proprietary ingredient which is an excipient (other than above in change EWI) | EWA | | 9D(3) |
| Quality control changes - FPS | Specification ranges – less restrictive | QFE | | 9D(3) |
| | Deletion of an existing test | QFU | | 9D(3) |
| | Analytical method – other than as specified above in change QFB | QFC | | 9D(3) |
| Quality control changes - SMS | Range – less restrictive | QSE | | 9D(3) |
| | Deletion of an existing test | QSU | | 9D(3) |
| | Analytical method – other than as specified above in change QSB | QSC | | 9D(3) |
| Packaging changes | Container material – other than in changes KBT, KGL or KBL | KOT | | 9D(3) |
| | Desiccant – inclusion in container | KDA | | 9D(3) |
| | Desiccant – removal from container | KDX | | 9D(3) |
| | Introduction of a package insert | KPI | C3 | 9D(3) |
| | Removal of a package insert | KRI | C3 | 9D(3) |
| | Introduction of a refill pack | KRP | | 9D(3) |

| Type of change | Change | Change code | Change code also in another Changes Table* | Relevant section of the TG Act |
|---|---|---|---|---|
| Manufacturing changes – finished product | Overseas manufacturer (includes site of manufacture), if GMP pre-clearance not provided | MOP | | 9D(3) |
| | Batch size for pressurised inhalation (nasal and oral respiratory) products | MBS | | 9D(3) |
| Product information | Introduction of a PI for an existing product | DPI | C3 | 9D(3) |
| | Changes other than the addition of more restrictive safety-related statements | DOT | C3 | 9D(3) |

## TGA changes table 3

Change types applicable for changed medicine applications lodged in Australia under application category C3

| Type of change | Change | Change code | Change code also in another Changes Table* | Relevant section of the TG Act |
|---|---|---|---|---|
| Label changes | Proprietary name (if grouping applies) | GPN | C2 | 23 |
| | New therapeutic indications (if grouping applies) | GIN | C2 & C4 | 23 |
| | Directions for use – e.g. dosage instructions (if grouping applies) (See also LIW) | GDU | C2 & C4 | 23 |
| | Changes on label (signal headings, warning statements) in compliance with new SUSDP requirements, where the change in scheduling is from 'Prescription Only Medicine' (Schedule 4) to a lower schedule | LSF | C2 | 9D(2) / 9D(3) |
| | Deletion or addition of text to the label (e.g. addition or removal of claims such as *clinically proven, fast/rapid action*; general claims regarding the product, its nature, mechanism of action, qualifying statements, etc.) | LDT | C2 | 9D(3) |
| Product detail changes | Proprietary name (if grouping applies) | GPN | C2 | 23 |
| | New therapeutic indications (if grouping applies) | GIN | C2 & C4 | 23 |
| Packaging changes | Introduction of a package insert | KPI | C2 | 9D(3) |
| | Removal of a package insert | KRI | C2 | 9D(3) |
| Product information | Introduction of a PI for an existing product | DPI | C2 | 9D(3) |
| | Changes other than the addition of more restrictive safety-related statements | DOT | C2 | 9D(3) |

*Dependent upon application category

## TGA changes table 4

Change types applicable for changed medicine applications lodged in Australia under application category C4

| Type of change | Change | Change code | Change code also in another Changes Table* | Relevant section of the TG Act |
|---|---|---|---|---|
| Label changes | New therapeutic indications (if grouping applies) | GIN | C2 & C3 | 23 |
| | Directions for use – e.g. dosage instructions (if grouping applies) (See also LIW) | GDU | C2 & C3 | 23 |
| Product detail changes | New therapeutic indications (if grouping applies) | GIN | C2 & C3 | 23 |

*Dependent upon application category

## Medsafe changes table 1

Change types applicable for changed medicine applications lodged in New Zealand under application category C1

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| Active Ingredient | Manufacturing process | 1 | tightening of limits for active substance | - |
| Excipient | Specifications/ test methods | 1 | revised specifications/test methods for a substance controlled according to a pharmacopoeial monograph (resulting from change to a different pharmacopoeia, not simply updating to the latest edition) | - |
| Finish product | Specifications/ test methods | 1 | revised specifications/test methods<br>no change in manufacturing process<br>product controlled according to a pharmacopoeial monograph (resulting from change to a different pharmacopoeia, not simply updating to the latest edition)<br>change in shape, engraving or coding of tablets<br>no change in dissolution or bioavailability | - |
| | Specifications/ test methods | 2 | tightening of limits for active substance<br>no other changes to specifications<br>no changes to test methods | - |
| | Specifications/ test methods | 3 | adoption of additional specifications/test methods not specified in the pharmacopoeial monograph for a product otherwise controlled according to a pharmacopoeial monograph | - |

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| Product stability and packaging | Shelf life/storage conditions | 1 | decrease in storage temperature from 30°C to 25°C with no change in shelf life and no other changes<br>addition of a statement such as "Protect from light" | (if applicable)<br>revised labelling and data sheet |
| | Container/ closure/ packaging | 1 | new pack size<br>evidence provided that stability study not required<br>no effect on dose measurement or dose delivery | (if applicable)<br>revised labelling and data sheet<br>revised packaging specifications |
| Datasheet | Miscellaneous changes | - | update or addition to safety information with no change to approved product details, and/or<br>expansion of pharmacokinetic and/or pharmacodynamic data, and/or<br>change in name or address of distributor with no change to approved product details | - |
| Labelling | - | 1 | re-design of label, and/or<br>change in name and address of distributor<br>no change to product name, strength, dose form, dosage instructions or indications | - |
| Sponsor | - | 1 | change of product sponsor from one company to another (not simply a change in the name or address of an existing sponsor) | (if applicable)<br>change of name and address of distributor on label and in data sheet |

## Medsafe changes table 2

Change types applicable for changed medicine applications lodged in New Zealand under application category C2

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| Product Name | Non-Umbrella Branded | - | new product name with no umbrella branding component associated with it to replace existing name<br>no change to formulation | (if applicable)<br>revised data sheet and labelling |
| Active Ingredient | Manufacturing site | - | new site of manufacture<br>manufacturing process unchanged | - |
| | Manufacturing process | 1 | new manufacturing process<br>Certificate of Suitability provided in lieu of DMF | (if applicable)<br>new site of manufacture |
| | | 2 | change in batch size, retest period, intermediate material supplier or specifications | - |
| | Specifications/ test methods | 2 | new specifications/test methods for a substance controlled according to a pharmacopoeial monograph (resulting from change to a different pharmacopoeia, not simply updating to the latest edition) | - |
| | | 3 | adoption of additional or different specifications/test methods not specified in the pharmacopoeial monograph for an active ingredient otherwise controlled according to a pharmacopoeial monograph | - |

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| | | 4 | revised specifications/test methods/testing protocol for a substance not controlled according to a pharmacopoeial monograph | - |
| Excipient | Specifications/ test methods | 2 | revised specifications/test methods for a Excipient substance not controlled according to a pharmacopoeial monograph | - |
| | | 3 | adoption of additional or different specifications/test methods not specified in the pharmacopoeial monograph for an excipient otherwise controlled according to a pharmacopoeial monograph | - |
| Finished Product | Packing site | 1 | new primary packing site that is not the site of manufacture and does not perform primary packaging<br>includes overlabelling | - |
| | | 2 | new primary packing site that is not the site of manufacture<br>new finished product testing site | - |
| | Specifications/ test methods | 4 | adoption of different specifications/test methods not specified in the pharmacopoeial monograph for a product otherwise controlled according to a pharmacopoeial monograph | - |

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| | | 5 | revised specifications/test methods<br>no change in manufacturing process<br>product not controlled according to a pharmacopoeial monograph | - |
| | Manufacturing process | 1 | type of manufacturing process unchanged, but changes to mixing times, batch scaling, type of equipment etc. | (if applicable)<br>revised specifications/test methods, new site of manufacture and packing |
| Product stability and packaging | Container/ closure/ packaging | 2 | new container or closure type and/or new pack size and/or new packaging material type<br>evidence provided that stability study not required<br>no effect on dose measurement or dose delivery | (if applicable)<br>revised labelling and data sheet<br>revised packaging specifications |
| | | 3 | new container or closure type and/or new pack size and/or new packaging material type<br>evidence provided that stability study not required<br>affects dose measurement or dose delivery | (if applicable)<br>revised labelling and data sheet<br>revised packaging specifications |
| | Shelf life/storage conditions | 2 | revised shelf life and/or storage conditions with no other changes | (if applicable)<br>revised labelling and data sheet |
| Indications and dosage | - | 4 | revised wording of indications/dosage with no actual change to indications or dosage | (if applicable)<br>revised data sheet and labelling |

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| | | 5 | new or revised indications/dosage for a multi-source medicine to match indications approved for innovator product | (if applicable)<br>revised data sheet and labelling |
| Labelling | - | 2 | design or re-design of a New Zealand compliant label and/or<br>change in the classification to Controlled Drug<br>no change in actual strength, but a change in the way the strength is expressed (if applicable) | - |
| | | 3 | request for a labelling exemption, or request for renewal of a labelling exemption | - |
| Formulation | - | 1 | change in overage of an active ingredient or excipient, or other excipient change where either:<br>the product is one for which comparative bioavailability data are not required; or<br>the change is not considered likely to affect bioavailability or stability | (if applicable)<br>new or revised specifications for excipient<br>revised specifications for finished product<br>revised labelling and data sheet<br>amended batch manufacturing documentation, provided there is no significant change in manufacturing process |

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| | | 2 | changed active ingredient salt, or change in status of ingredient from active to excipient, or removal of active ingredient with no other changes<br><br>change not considered likely to affect stability | (if applicable)<br><br>new specifications/test methods for active ingredient and finished product<br><br>revised labelling and data sheet<br><br>amended batch manufacturing documentation, provided there is no significant change in manufacturing process |

## Medsafe changes table 3

Change types applicable for changed medicine applications lodged in New Zealand under application category C3

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| Product Name | Umbrella Branded | - | new product name with umbrella branding component associated with it to replace existing name<br>no change to formulation | (if applicable)<br>revised data sheet and labelling |

## Medsafe changes table 4

Change types applicable for changed medicine applications lodged in New Zealand under application category C4

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| Formulation | - | 3 | changed active ingredient salt or removal of active ingredient with no other changes, stability study included (where bioequivalence data is not required) | (if applicable)<br>new specifications/test methods for active ingredient and finished product<br>revised labelling and data sheet<br>amended batch manufacturing documentation, provided there is no significant change in manufacturing process |
| | | 4 | excipient change that may affect, or is considered likely to affect, bioavailability, stability or safety | (if applicable)<br>new or revised specifications/test methods for excipient<br>revised labelling and data sheet |
| Active Ingredient | Manufacturing process | 2 | new manufacturing process<br>DMF or equivalent documentation supplied (Module 3.2.S) | (if applicable)<br>process validation for active ingredient<br>revised specifications/test methods for active ingredient<br>new site of manufacture |

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| Finished Product | Manufacturing process | 2 | new type of manufacturing process | (if applicable)<br>revision or reconfirmation of shelf life<br>revised specifications/test methods<br>new site of manufacture and packing |
| Product stability and packaging | Container/ closure/ packaging | 4 | new container or closure type and/or new pack size and/or new packaging material type<br>revised shelf life and/or storage conditions (stability study included)<br>does not affect dose measurement or dose delivery | (if applicable)<br>revised labelling and data sheet<br>revised packaging specifications |
| | | 5 | new container or closure type and/or new pack size and/or new packaging material type<br>revised shelf life and/or storage conditions (stability study included)<br>affects dose measurement or dose delivery | (if applicable)<br>revised labelling and data sheet<br>revised packaging specifications |
| Indications and dosage | - | 1 | new indication, supporting clinical data required<br>Note: CMN will generally be referred under section 24(5). | (if applicable)<br>new dosage instructions<br>revised data sheet and labelling |
| | | 2 | modified indication<br>supporting clinical data required<br>Note: CMN will generally be referred under section 24(5). | (if applicable)<br>new dosage instructions<br>revised data sheet and labelling |

| Category | Sub Category | Grade | Change | Consequential Changes |
|---|---|---|---|---|
| | | 3 | new dosage regimen<br>no change to indications<br>supporting clinical data required | (if applicable)<br>new dosage instructions<br>revised data sheet and labelling |
| Contraindications, Warning and Precautions | | 1 | relaxation of contraindications, and/or<br>relaxation of warnings and precautions regarding use in pregnancy, lactation or particular population/patient subgroups,<br>supporting clinical data required | (if applicable)<br>revised data sheet and labelling |

# Appendix 4: OTC BPR glossary

## A

**ACNM - Advisory Committee on Non-prescription Medicines**

An Australian technical advisory committee to advise and make recommendations to the TGA regarding the entry of non-prescription medicines on the Australian Register of Therapeutic Goods (the Register).

**Active Ingredient**

A therapeutically active substance included in a medicine.

**ARGOM - Australian Regulatory Guidelines for OTC Medicines**

Australian guidelines which describe the information to be supplied with an application for registration of an OTC Medicine in the ARTG.

**ARTG - Australian Register of Therapeutic Goods**

The publicly accessible reference database of the therapeutic goods that have been approved for marketing in Australia.

**ANZTPA - Australia New Zealand Therapeutic Products Agency**

The Australian and New Zealand Governments have agreed to proceed with a joint scheme for regulation of therapeutic products (i.e. medicines, medical devices, etc.) that is anticipated to be operational from 2016.

Over time, the joint arrangements will be administered by a single regulatory agency, the Australia New Zealand Therapeutic Products Agency, which will absorb the current regulators - Australia's Therapeutic Goods Administration and New Zealand's Medsafe.

## C

**Clone**

An OTC medicine that is identical in all respects to an existing approved medicine, apart from the product name and identifying details on the product label.

**CTD - Common technical document**

A set of specifications for an application dossier for the registration of a medicines maintained by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Additional information on the CTD requirements can be obtained at: http://www.ich.org/products/ctd.html.

## D

**Data sheet**

A New Zealand-specific document that contains information relating to the safe and effective use of the medicine, including information regarding the usefulness and limitations of the medicine (known in Australia as the product information).

## G

**Generic medicine**

A medicine that, in comparison to an existing medicine:

- has the same quantitative composition of therapeutically active substances, being substances of similar quality to those used in the registered medicine; and
- has the same pharmaceutical form; and

- is bioequivalent; and
- has the same safety and efficacy properties

**GMP - Good manufacturing practice**

A set of principles and procedures which, when followed by manufacturers of therapeutic goods, helps ensure that the products manufactured will have the required quality.

**GMP clearance**

The TGA-specific approval of GMP documentary evidence that shows the medicine is being manufactured to an acceptable standard

## H

**House brand**

A range of medicines where the umbrella segment of the medicine's name is typically associated only with the sponsor or retailer.

## I

**Indications**

Specific therapeutic uses of the medicine.

## L

**Label**

A display of printed information:

- on or attached to the medicine; or
- on or attached to a container or primary pack in which the medicine is supplied; or
- supplied with such a container or pack

## M

**MAAC – Medicines Assessment Advisory Committee**

A New Zealand technical advisory committee that advises the New Zealand Minister of Health on the risk-benefit profile of new medicines.

## N

**NZRGM - New Zealand Regulatory Guidelines for Medicines**

Guidance notes for applicants for consent to distribute new and changed medicines and related products in New Zealand.

**New Zealand Label Statements Database**

The New Zealand-specific document that specifies all mandatory label advisory statements for medicine labels.

## O

**OMM - OTC Medicine Monograph**

A document, relating to a specific active ingredient that specifies the requirements for a new medicine application to enable evaluation via the N5 category.

**OTC - Over-the-Counter medicine**

A medicine that can be purchased without a prescription as a Pharmacist only, Pharmacy only or General sale

# P

### PI - Product Information

An Australian-specific document that contains information relating to the safe and effective use of the medicine, including information regarding the usefulness and limitations of the medicine (known in New Zealand as a data sheet).

# R

### RASML - Required Advisory Statement for Medicine Labels

An Australian-specific document that specifies all mandatory label advisory statements from the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) and the Therapeutic Goods Regulations.

### RFI – Request for Information Letter

Letter from the regulator detailing points for clarification, and/or outstanding data requirements for an application in progress.

# S

### Sponsor

The individual or body corporate that is legally responsible for distribution of a medicine. Sponsor responsibilities are further defined within the *Therapeutic Goods Act 1989*, in Australia, and the *Medicines Act 1981*, in New Zealand.

### Stakeholder

A person, group or organisation that has an interest in or can affect or is affected by an organisation's actions.

### SUSMP - Standard for the Uniform Scheduling of Medicines and Poisons

The Australian-specific document that specifies certain legal requirements for the labelling of poisons and medicines for sale to the public in Australia. (Also known as the Poisons Standard)