Australian Government
Department of Health
Therapeutic Goods Administration

Mandatory requirements for an effective over-the-counter medicines application

Applicable for applications lodged from 1 March 2016

Version 1.2, July 2021

TGA Health Safety Regulation

Contents

Overview

This document describes the information (and the form of that information) that must be submitted to the TGA in order for an application to register an over-the-counter (OTC) medicine to be considered effective and proceed to evaluation.

Scope

These requirements apply to applications to register an OTC medicine that are lodged with the TGA from 1 March 2016, including applications to change a registered OTC medicine that result in a separate and distinct good under subsection 16(1) of the *Therapeutic Goods Act 1989* (the Act) to which the *Therapeutic Goods (Groups) Order No. 1 of 2001* applies.

Background

Applications for new registrations

Applications for new registrations[1] are made under *section 23 of the Act*. Section 23 requires that applications:

- are made in accordance with a form or in a manner approved by the Secretary (subsection 23(1) of the Act); and
- include such information in a form approved by the Secretary as will allow the determination of the application (paragraph 23(2)(b) of the Act); and
- for restricted medicines, include product information in the form approved under section 7D of the Act (paragraph 23(2)(ba) of the Act).

Section 23 instruments

The section 23 instruments specify how applications to register an OTC Medicine must be made and require applications to include the information described in the following regulatory documents in order to be effective and proceed to evaluation:

- Mandatory requirements for an effective over-the-counter application (this document)
- CTD Module 1: OTC medicines.

[1] A new registration is one that requires a new ARTG entry by reason of being separate and distinct goods under section 16 of the *Therapeutic Goods Act 1989*. This includes new chemical entities, new strengths, new dosage forms, different directions for use, formulation changes, changes in trade name, extension of indication etc. Under the Therapeutic Goods (Groups) Order 2001, not all new registrations will result in a new AUST R number being allocated if the existing medicine is 'grouped' with the new medicine.

OTC medicine applications

For information on the OTC application levels that are referred to in this document, and the application process, go to:

- Determining the correct application level for OTC medicine submissions
- OTC New medicine registration process
- Process to change a registered OTC medicine
- Changing an OTC medicine: using the changes table.

Mandatory requirements

Organisation and format of the application dossier

The applicant must provide an application dossier that has been completed and structured in accordance with the relevant instructions specified in:

- CTD Module 1: OTC medicines: Completed to the extent that it is applicable for all OTC application levels.
- Module 2: Overviews, written summaries and tabulated summaries of the data contained in the Modules 3, 4 and 5. Completed to the extent that it is applicable for particular N3, N4, N5, C3 and C4 applications, as detailed in Appendix A: Specific mandatory requirements (Module 2).
- Module 3: ICH M4Q Common technical document for the registration of pharmaceuticals for human use - Quality (CPMP/ICH/2887/99 Rev 1 Quality). Completed to the extent that it is applicable for particular N1, N2, N3, N4, N5, and C2 applications, as detailed in Appendix A: Specific mandatory requirements (Module 3).
- Module 4: ICH M4S Common technical document for the registration of pharmaceuticals for human use - Safety (CPMP/ICH/2997/99 Rev 1 Safety). Completed to the extent that it is applicable for particular N4, N5, C3 and C4 applications, as detailed in Appendix A: Specific mandatory requirements (Module 4).
- Module 5: ICH M4E Common technical document for the registration of pharmaceuticals for human use - Efficacy (CPMP/ICH/2887/99 Rev 1 Efficacy). Completed to the extent that it is applicable for particular N4, N5, C3 and C4 applications, as detailed in Appendix A: Specific mandatory requirements (Module 5).

The application dossier must be submitted electronically, in accordance with the requirements in the General dossier requirements.

Content of the application dossier

The application dossier must provide appropriate documentation (in the correct format and locations, as determined by the CTD modules) to allow a delegate of the Secretary to decide whether the medicine can be approved for registration on the Australian Register of Therapeutic Goods (ARTG). The exact content of the application dossier will vary according to the application level and type of medicine.

Technical data requirements

The technical information that is required in Module 2, 3, 4 and 5 for an application to be considered effective is at Appendix A – Specific technical data requirements.

Where an application meets the description of more than one of the application types listed in *Appendix A – Specific technical data requirements,* data must be provided in accordance with the requirements for each application type that is relevant to the application.

Australia-specific and adopted European Union and ICH guidelines

It is the applicant's responsibility to identify and familiarise themselves with the relevant Australia-specific guidelines and adopted European Union (EU) and ICH guidelines.

The use of European Union (EU) and ICH guidelines adopted in Australia and other Australia-specific guidelines is not mandated in the legislation. However, under paragraph 25(1)(d) of the Act the delegate is required, when evaluating an application for registration, to consider:

> *"…whether the quality, safety, and efficacy of the goods for the purposes for which [the goods] are to be used have been satisfactorily established."*

Australia-specific guidelines and adopted EU and ICH guidelines describe the kind of data and information to be included in each Module of a dossier to demonstrate quality, safety, and efficacy. If the dossier does not contain all of this information, the TGA may not be able to determine whether the quality, safety and efficacy of the medicine has been satisfactorily established.

Please note

The TGA has an ongoing process to consider newly released and updated EU and ICH guidelines and decide whether or not to adopt them. As part of this process, some of the above guidelines may be amended, removed or replaced from time to time. Applicants should check the TGA website routinely and subscribe to the email list to receive updates on new content.

Justification for not complying with technical data requirements and not adhering to guidelines

Compliance with relevant requirements set out in Appendix A – Specific technical data requirements and adherence to applicable guidelines is highly desirable as it most readily allows the TGA to come to a view as to whether the medicine can be registered on the ARTG.

Where there are any deviations from relevant requirements or applicable guidelines, the applicant must advise the TGA and provide a justification.

When a justification needs to be provided

If the application does not meet a specific technical requirement or does not adhere to an applicable guideline, a justification must be provided.

For instance, a justification must be provided when:

- the dossier does not contain a Module that is required for the application to be considered effective and accepted for evaluation.
- the application does not adhere, either in full or in part, to the guidelines that set out the required technical information.

What needs to be included in a justification

Where the TGA has provided detailed information to assist applicants to construct a justification, ensure **all** details have been addressed in the justification. For example, the TGA Biopharmaceutic studies guideline provides information on the required content for a justification for not conducting biopharmaceutic studies.

In other cases, applicants need to make a separate robust scientific justification for each deviation from relevant data requirements or applicable guidelines. The justification must include all of the following for the application to be effective:

- the requirement, guideline or part of the guideline that is not being met must be identified and explain how it is not being met;
- detail of the proposed alternative approach and a contemporary scientific justification for why the approach is valid, with reference to supporting documents;
- citations of the relevant reference documents, including TGA documents, where appropriate;
- literature based submissions must be in accordance with TGA guidance on Literature based submissions and the OTC medicines – Safety and efficacy data;
- copies of all cited references documents (other than TGA documents) in the dossier.

Purpose of the justification

Each justification performs two functions:

- it needs to be present and address all of the above points for each relevant requirement that is not met or applicable guideline that is not adhered to, in order for the application to be considered effective under section 23 of the Act and be accepted by the TGA for evaluation; and
- once the application has been accepted for evaluation, each justification needs to be sufficient for the TGA to be satisfied that the medicine can be registered on the ARTG. The content and merit of a justification (i.e. whether the alternative approach is in fact valid) will be assessed during the evaluation phase.

Compliance with administrative requirements

Applicants must comply with, and cannot provide a justification for not complying with, administrative requirements as set out in:

- this document; Organisation and format of the application dossier
- CTD Module 1: OTC medicines
- General dossier requirements
- the approved application forms in TGA Business Services

Appendix A - Specific technical data requirements

Where an application meets the description of more than one of the application types listed in this appendix, data must be provided in accordance with the requirements for each application type that is relevant to the application. Where these tables refer to the data requirements described in European Union (EU) guidelines that have been adopted by the TGA, the guidance should be read in conjunction with any applicable TGA annotation.

Table 1: Module 2 - CTD summaries

CTD Module	OTC Application level	Requirement	Table reference number
2.3 Quality overall summary	N5 (new active ingredients only)	Provide Module 2.3 completed in accordance with ICH M4Q Common technical document for the registration of pharmaceuticals for human use - Quality (CPMP/ICH/2887/99 Rev 1 Quality). Module 2.3 is not required for other N5 level applications.	1.a
2.4 Nonclinical overview	N4, N5, C3, C4	For all applications that include Module 4, provide Module 2.4 completed in accordance with ICH M4S Common technical document for the registration of pharmaceuticals for human use - Safety (CPMP/ICH/2887/99 Rev 1 Safety). Also provide Module 2.4 for applications where the levels of impurities and degradants lie outside the levels permitted in Guidelines on quality aspects of OTC applications (these applications require Module 4 data in support of the proposed limits or a justification for the absence of Module 4 data).	1.b
2.5 Clinical overview	N4, N5, C3, C4	For all applications that include Module 5, provide Module 2.5 completed in accordance with ICH M4E Common technical document for the registration of pharmaceuticals for human use - Efficacy (CPMP/ICH/2887/99 Rev 1 Efficacy) to the extent that it is applicable. For example, for a generic medicine application where Module 5 only consists of a bioequivalence study (Module 5.3.1), Module 2.5 would consist of a clinical overview of the findings from the bioequivalence study together with any other relevant information, as appropriate.	1.c

CTD Module	OTC Application level	Requirement	Table reference number
2.6 Nonclinical summary	N4, N5, C3, C4	For all applications that include Module 4, provide Module 2.6 completed in accordance with ICH M4S Common technical document for the registration of pharmaceuticals for human use - Safety (CPMP/ICH/2887/99 Rev 1 Safety).	1.d
2.7 Clinical summary	N4, N5, C3, C4	For all applications that include Module 5, provide Module 2.7 completed in accordance with ICH M4E Common technical document for the registration of pharmaceuticals for human use - Efficacy (CPMP/ICH/2887/99 Rev 1 Efficacy) to the extent that it is applicable. For example, for a generic medicine application where Module 5 only consists of a bioequivalence study (Module 5.3.1), Module 2.7 would consist of a clinical summary of the bioequivalence study.	1.e

Table 2: Module 3 - Quality

The table below describes the minimum data that must be submitted in Module 3 for an application to be considered effective. For further guidance refer to the Guidelines on quality aspects of OTC medicines.

CTD Module	OTC Application level/type	Module 3 requirement	Table reference number
3.2.S Drug Substance	N5 – new active ingredient	For an application to register a medicine containing a new chemical entity that is an active ingredient, provide Module 3.2.S data in accordance with the Mandatory requirements for an effective application for prescription medicines.	2.a
3.2.S.4 Drug substance (Control)	N3, N4, N5 – excluding new active ingredients and premixes	For a drug substance that is the subject of a default standard monograph provide, either: • Confirmation that the **full** specifications (test methods and limits) detailed in the relevant monograph in the default standard (BP/Ph.Eur or USP) are applied and no additional critical control parameter tests are necessary to ensure the quality of the medicine, e.g. particle size of the active for inclusion in a suspension; or • The proposed drug substance specifications and: – a justification for any non-pharmacopeial tests and limits. – details of non-pharmacopeial test methods. For a drug substance that is NOT the subject of a default standard monograph provide: • The proposed drug substance specifications and: – a justification for the tests and limits. – details of the test methods.	2.b

CTD Module	OTC Application level/type	Module 3 requirement	Table reference number
Drug substance (control)	N3, N4, N5 – premixes (ingredient blends)[2]	For a drug substance that is purchased already manufactured as part of an ingredient blend or premix, provide: • The finished product manufacturer's acceptance specifications for the ingredient blend or premix. • A justification for the tests and limits. • Confirmation that all components of the blend or premix are of appropriate pharmaceutical grade and comply with any relevant default standards.	2.c
3.2.P.1 & 3.2.P.2 Drug product (description, composition and pharmaceutical development)	N3, N4, N5	• Define the composition of the medicine and role of the ingredients. • Provide details and a justification for any overage applied during manufacture. • If tablets are scored, provide data to confirm that splitting is clean and the portions produced comply with pharmacopoeial limits for uniformity of weight/content. • Provide full details of pharmaceutical development for: – Modified release dosage forms – N5 applications for new strengths, new dosage forms, new fixed combination medicines or new chemical entities.	2.d

[2] For more information on proprietary ingredient mixtures that contain an active ingredient see Streamlining proprietary ingredient categories.

CTD Module	OTC Application level/type	Module 3 requirement	Table reference number
3.2.P.3 Drug product (manufacture)	N3, N4, N5	Include a brief outline of the method of manufacture and batch formula. Provide an assurance that the manufacturing process will be validated (or has been validated) according to the requirements of the Code of Good Manufacturing Practice [the Therapeutic Goods (Manufacturing Principles) Determination No. 1 2013 contains a definition of 'the Code'], and that the manufacturer's validation report and related information will be available for review, on request, by the TGA within 3 months of release for supply of the first production batch. Additional manufacturing validation information is required for the following specific medicine types: • For oral dosage forms where the active ingredient is present at less than 2 mg or 2% w/w (microdose) the full manufacturer's process validation report must be provided. • For metered dose inhalers, novel dosage forms, sustained release medicines (excluding enteric coated medicines) and nasal corticosteroids, provide the manufacturer's process validation report (or a summary of the report) including the critical steps in the manufacturing process and the manufacturer's analysis and conclusions. • For sterile medicines, provide validation data that covers the following: – for all sterile medicines, bioburden information including presterilisation bioburden limits and for extended processing times (including hold times), evidence to show that sterility or microbiological quality (as applicable) is not compromised **Note:** the TGA has the expectation that bioburden information including a specification for pre-sterilisation bioburden limits will be provided for all applications for market authorisation, not just for those with certain sterilisation procedures. • For medicines that are sterilised by filtration and aseptically filled or aseptically manufactured the following validation data (as applicable): – containers/closures: ▪ parameters of the sterilisation processes and confirmation that these have been physically and microbiologically validated to a SAL of 10-6 ▪ statement that processes to remove endotoxin have been validated to demonstrate a reduction in endotoxin units of > 3-log	2.e

CTD Module	OTC Application level/type	Module 3 requirement	Table reference number
		– sterilising filter: ▪ confirmation that the membrane filter is tested for integrity before and after use ▪ validation of the bacterial retention capabilities of the filter conducted in the presence of the product – statements of maximum permitted processing (holding, storage and filling times) during manufacture – media fill studies to validate the aseptic manufacturing process. Media fill studies should be conducted under worst case conditions including maximum processing and filling times, and should include simulation of all aseptic manufacturing processes, including those using previously sterilised components • For terminally sterilised medicines or sterilised drug substances or excipients not subjected to further sterilisation: – physical and microbiological performance qualification studies and confirmation that these studies show that a SAL of 10-6 is achieved throughout the maximum and minimum loads – statements of processing times (e.g. from start of compounding until terminal sterilisation).	
3.2.P.4 Control of excipients	N1 (flavour/fragrance /colour variants only) C2 change code GPI - addition of flavour/fragrance /printing ink or colouring.	Provide the proposed specifications and details of the test methods for the new flavour/fragrance/colours(s).	2.f

CTD Module	OTC Application level/type	Module 3 requirement	Table reference number
3.2.P.4 Control of excipients	N3, N4, N5	State which excipients comply fully with the applicable monograph in the default standard (BP/Ph.Eur. or USP). For excipients that are the subject of a default standard monograph, provide either: • Confirmation that the **full** specifications (test methods and limits) detailed in the relevant monograph in the default standard (BP/Ph.Eur or USP) are applied and no additional critical control parameter tests are necessary to ensure the quality of the medicine; or • The proposed specifications and: – a justification for any non-pharmacopoeial tests and limits. – details of non-pharmacopoeial test methods. For excipients that are NOT the subject of a default standard monograph, provide: • The proposed specifications and: – a justification for the tests and limits. – details of the test methods. For excipients that are purchased already manufactured as part of a premix (ingredient blend), provide: • The finished product manufacturer's acceptance specifications. • A justification for the tests and limits. • Confirmation that all components of the blend or premix are of appropriate pharmaceutical grade and comply with any relevant default standards.	2.g
3.2.P.5.1 Control of drug product	N2, N3, N4, N5	Provide the proposed expiry and release specifications for the finished product. **Note:** Finished product specifications must be provided for all N2, N3, N4 and N5 applications, including those where a justification is made for providing an abridged Module 3 (for example, when all quality aspects are identical to a fully evaluated 'parent' medicine, whose sponsor has given the TGA authorisation to access the parent files for the purpose of the application).	2.h

CTD Module	OTC Application level/type	Module 3 requirement	Table reference number
3.2.P.5.2 Analytical procedures	N3, N4, N5	Provide a detailed description of all in-house test methods, in accordance with the requirements of the Guidelines on quality aspects of OTC medicines – *Analytical procedures and validation*.	2.i
3.2.P.5.3 Validation of test methods	N3, N4, N5	Provide analytical validation reports for critical assay methods, in accordance with the requirements of the Guidelines on quality aspects of OTC medicines – *Analytical procedures and validation*. All raw data supplied (e.g. HPLC traces) must be clear and legible.	2.j
3.2.P.5.4 Batch analysis	N2, N3, N4, N5	Provide certificates of analysis for at least two batches.	2.k
3.2.P.5.6 Control of drug product	N3, N4, N5	Provide a justification for the finished product specifications including: • a justification in terms of safety for any impurity limits that are above those specified in the *Guidelines on quality aspects of OTC medicines* (refer to Table 1 and Table 3 for the relevant Module 2.4 and Module 4 requirements). **Note:** The finished product specifications must ensure compliance with all applicable default standard requirements and Therapeutic Goods Orders.	2.l
3.2.P.7 Container closure system	N2, where a measuring device is supplied with the medicine.	Provide details of the calibrations on the measuring device.	2.m
3.2.P.7 Container closure system	N3, N4, N5	• Provide details of the container and measuring or dose delivery devices, including: – details of the materials and specifications – technical drawings of dose delivery/measuring device, where design, composition and performance of the device is not clearly described in the submitted specifications (including details of the calibrations).	2.n

CTD Module	OTC Application level/type	Module 3 requirement	Table reference number
		• For plastic and rubber packaging components of the primary packaging provide evidence that the components comply with relevant BP/Ph. Eur and/or USP/NF requirements for polymeric materials used in packaging medicines or, if appropriate, are approved for use with foodstuffs. • If the medicine is subject to the Therapeutic Goods Order No 80 *Child-resistant Packaging Requirements for Medicines* (TGO 80) provide an assurance that the container closure system complies with the Therapeutic Goods Order No 80 *Child-resistant Packaging Requirements for Medicines*. • For medicines supplied with a measuring device, provide an assurance that it complies with the requirements for *Uniformity of Weight (Mass) of Delivered Doses from Multidose Containers* in the BP/Ph.Eur Appendix XII C. *Consistency of Formulated Preparations.*	
3.2.P.8 Stability	N3, N4, N5	Provide information regarding stability trials in accordance with the requirements of the Guidelines on quality aspects of OTC medicines, including: • A tabular stability summary and conclusions in regard to the storage conditions and shelf-life. • A statement of which batches are identical to those intended for marketing in terms of formulation, container, and manufacture. Provide details and justification for any differences between the stability batches and the proposed medicine. • A post-approval stability commitment to conduct full term stability testing on at least two production batches (if required). • Full details of stability testing conducted on each individual strength, container type and size of the medicine (unless bracketing or matrixing is applied), in accordance with the relevant CPMP/ICH guidelines and associated TGA annotations. – Results must be in tabular format. – Confirm that the test methods used in the stability study are the same as those provided in 3.2.P.5 Control of the Drug Product or, if this is not the case, provide detailed stability study test methods and analytical validation data.	2.o

CTD Module	OTC Application level/type	Module 3 requirement	Table reference number
		– If there were any changes in test procedures during the course of the trials, provide comparison and correlation of results generated by the alternative methods. – For conventional dosage forms where the active ingredient is known to be stable, provide no less than 6 months long term and accelerated stability data on a minimum of two batches of at least pilot scale. – For unconventional dosage forms (including modified release) or for medicines that are likely to be unstable or contain a new active ingredient, provide no less than 12 months long term and 6 month accelerated stability data on a minimum of three batches, of which two must be at least pilot scale. – Provide results of microbiological contamination testing or, where relevant, sterility testing. – For solid dosage forms in potentially moisture-permeable packaging, provide high humidity stability data. – For non-solid dosage forms in potentially moisture-permeable packaging, provide low humidity stability data. – For multi-dose liquid or semi-solid medicines provide: ▪ antimicrobial preservative efficacy data at the beginning and end of the closed shelf life, as specified in TGO 77 Microbiological Standards for Medicines ▪ information to support the in-use period, e.g. microbiological challenge testing/simulated use testing. – For oral solid dosage forms or suspensions that make 'fast' or 'rapid' claims on the labels, provide dissolution data in accordance with the Guideline on presentation aspects of OTC applications – Fast or rapid claims. If the stability data package does not meet any or all of the above requirements, this must be identified in the application cover letter and a justification must be included that meets the requirements detailed above in Justification for not complying with technical data requirements.	

Table 3. Module 4—Safety (nonclinical study reports)

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 4 requirement	Table reference number
Application for a medicine that contains an excipient that is one or more of: • a new chemical entity (i.e. not on the TGA Ingredient tables) • not approved for use in OTC medicines • a new route of administration • at a higher concentration or daily dose than has been approved for that route of administration. **Note:** If you are unsure whether the excipient has been assessed for the proposed route of administration, concentration or OTC use, contact otc.medicines@tga.gov.au	N4, N5, C3	4	Provide nonclinical data or a justification for not providing data, in accordance with the: • *OTC medicines – Safety and efficacy data - (non-clinical studies).* • *Guidelines on OTC applications for new substances* An assessment of the information relating to safety must be provided in the nonclinical overview (Module 2.4).	3.a
Application for a medicine that has impurities that are above those allowed without justification in the *Guidelines on quality aspects of OTC Medicines*.	N4, N5	4	Provide safety data (Module 4) or a scientific justification (Module 2.4 and/or Module 4) to support the proposed impurity limits. Provide an assessment of this information in the nonclinical overview (Module 2.4).	3.b
Applications that are fully or partly literature based (literature based submission).	N4, N5, C3, C4	4.3	Provide information in accordance with the TGA guidance: • literature based submissions and; • *OTC medicines - Safety and efficacy data* Note. Modules 1.5.1, 2.4 and 2.6 (as applicable) are also required.	3.c

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 4 requirement	Table reference number
Applications for a topical medicine that includes a 'hypoallergenic' claim.	N4, N5	4	Provide data in accordance with the requirements detailed in the Guidelines on OTC applications for specific substances – Hypoallergenicity of topical preparations.	3.d
Application for a non-generic medicine that has one or more of: • a new chemical entity that is an active ingredient including; – new salt or ester – new isomer/ mixture of isomers • a new combination of active ingredients • a new route of administration of the active ingredient • higher dosages of the active ingredient or use over a longer period of time • a new strength • a different patient population	N5, C4	4	Provide nonclinical data or a scientific justification for the absence of nonclinical data, in accordance with: • The OTC medicines – Safety and efficacy data • The *Guidelines on OTC applications for new substances*, for new active ingredients, new routes of administration or higher dosages. Provide an assessment of the information relating to safety in the nonclinical overview (Module 2.4).	3.e

Table 4: Module 5 - Efficacy (clinical study reports): General application requirements

In addition to the requirements in this table, the specific Module 5 requirements for generic medicine applications are described in Table 5, and for non-generic medicine applications in Table 6.

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 Requirement	Table reference number
Applications that include comparative bioavailability/ bioequivalence reports	N4, N5, C4	5.3.1	Provide bioavailability/bioequivalence study reports in accordance with requirements detailed in: • Guideline 15: Biopharmaceutic studies • OTC medicines – Safety and efficacy data **Note:** • The Australian originator reference medicine used in the studies must have been registered on the basis of a full dossier, which may include chemical, biological, pharmaceutical, pharmacological-toxicological and clinical data. • The bioavailability/bioequivalence summary is placed in Module 1.11	4.a
Applications that include reports of biopharmaceutic studies using overseas reference product	N4, N5, C4	5.3.1	For a biopharmaceutic study using an overseas reference product, provide data in accordance with requirements detailed in Guideline 15: Biopharmaceutic studies – Choice of the reference product for bioequivalence of generic medicines).	4.b
Applications that are fully or partly literature based (literature based submission).	N4, N5, C4	5.4	Provide information in accordance with the TGA guidance: • Literature based submissions, and • OTC medicines – Safety and efficacy data **Note:** Module 1.5.1, 2.5 and Module 2.7 and copies of all references will need to be provided.	4.c

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 Requirement	Table reference number
Applications for locally acting, locally applied medicines that include studies using pharmacodynamic endpoints.	N4, N5, C4	5	Provide data demonstrating that the pharmacodynamic model is internally and externally valid. The use of pharmacodynamic endpoints must be justified in terms of their direct relevance to the intended therapeutic effect of the active ingredient in the medicine. **Note:** An example of a pharmacodynamic endpoint that is **not** related to therapeutic effect of the medicine is the vasoconstrictor assay referred to in the guideline Clinical Investigation of corticosteroids intended for use on the skin. The vasoconstrictor assay endpoint may not be externally valid when the composition of the generic medicine differs from the reference.	4.d
Applications to include a 'fast' or 'rapid' claim as part of the medicine name or a 'fast/ faster absorption' claim.	N4, N5, C4, C3	5	Provide supporting clinical efficacy data or pharmacokinetic data in accordance with the Guideline on presentation aspects of OTC applications – Fast or rapid claims.	4.e

Table 5. Module 5—Efficacy (clinical study reports): N4 application requirements (generic medicines)

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 requirement	Table reference number
Generic oral medicines, other than those specifically excluded from requiring bioequivalence data in the guidance *OTC medicines – Safety and efficacy data. When bioequivalence data (or justification) are not required.*	N4	5.3.1	Provide bioavailability/bioequivalence study reports in accordance with the requirements for generic medicines detailed in: • OTC medicines – Safety and efficacy data – Generic oral medicines • Guideline 15: Biopharmaceutic studies	5.a
Generic modified release oral medicine.	N4	5.3.1	Provide the bioavailability/bioequivalence study reports in accordance with the requirements detailed in: • OTC medicines – Safety and efficacy data • *Guidance on the pharmacokinetic and clinical evaluation of modified release dosage forms* (EMA/CPMP/EWP/280/96 Corr1).	5.b
Generic topical medicines	N4	5.3.4 5.3.5	Provide data demonstrating therapeutic equivalence with a corresponding Australian originator medicine, in accordance with the requirements detailed in: • OTC medicines – Safety and efficacy data – Generic topical (locally *acting, locally applied)* medicines	5.c

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 requirement	Table reference number
Generic nicotine replacement therapy	N4	5	Provide data in accordance with: • the requirements detailed in the Guidelines on OTC applications for specific substances – Nicotine replacement therapy • OTC medicines – Safety and efficacy data	5.d
Generic antiseptic for: • First aid • Use in the mouth	N4	5.3	Provide *in vitro* data demonstrating the antimicrobial activity using the following suitable test methods (as relevant): • The *in vitro* test described in the FDA Tentative Final Monograph for first aid antiseptic products • The TGA disinfectant test (option D) for antiseptics modified to make it a quantitative method and supported by adequate validation data. • The FDA Tentative Final Monograph for oral antiseptic drug products • FDA proposed monograph for antigingivitis /antiplaque drug products	5.e
Generic antiseptic: • Handwashes or handrubs • Patient preoperative skin preparations • Surgical hand disinfectants	N4	5.3	Provide *in vitro* and *in vivo* data demonstrating the efficacy using the following suitable test methods (as relevant): • The European Standard EN13727 for chemical disinfectants and antiseptics. • FDA Tentative Final Monograph for health-care antiseptic drug products • The European Standard EN 1499 for hygienic handwashes. • The European Standard EN 1500 for hygienic handrubs • The European standard EN 12791 for surgical hand disinfectants	5.f

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 requirement	Table reference number
Generic head lice treatment	N4	5.3	Provide data in accordance with: • Guidelines on OTC applications for specific substances – Head lice treatments. • OTC medicines – Safety and efficacy data	5.g

Table 6. Module 5—Efficacy (clinical study reports): N5 and C4 application requirements (non-generic medicines)

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 requirement	Table reference number
New strength	N5	5.3.1	• For medicines that are systemically absorbed (e.g. oral tablets), provide comparative bioavailability/bioequivalence study reports in accordance with: – *Guideline 15: Biopharmaceutic studies* • For locally applied, locally acting medicines, provide data in accordance with the EU document *Clinical requirements for locally applied, locally acting products containing known constituents* (pp. 193–8 of Rules 1998 (3C) – 3CC12a). If the new strength is associated with new indications, dosage, directions for use or target population, also provide data in accordance with the *OTC medicines – Safety and efficacy data* and any other specific Australian or EU guidelines relevant to the medicine.	6.a
New dosage form.	N5	5.3.1	Provide data in accordance with: • the guidance OTC medicines – Safety and efficacy data • any other specific Australian or EU guidelines relevant to the medicine. For example, for systemically absorbed dosage forms provide study reports in accordance with *Guideline 15: Biopharmaceutic studies*.	6.b
New modified release dosage forms.	N5	5	Provide data in accordance with: • OTC medicines – Safety and efficacy data • Any other specific Australian or European Union (EU) guidelines relevant to the medicine, including the *Guidance on the pharmacokinetic and clinical evaluation of modified release dosage forms* (EMA/CPMP/EWP/280/96 Corr1).	6.c

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 requirement	Table reference number
New route of administration.	N5	5	Provide data in accordance with: • the guidance OTC medicines – Safety and efficacy data • any other specific Australian or EU guidelines relevant to the medicine.	6.d
New indications, dosage, directions for use or target population.	N5 C4 (change code GID or GDD)	5	Provide data in accordance with: • the guidance OTC medicines – Safety and efficacy data • any other specific Australian or EU guidelines relevant to the medicine.	6.e
New fixed combination medicine or composite packs containing multiple active ingredients that do not contain a new active ingredient (new chemically entity).	N5	5	Provide data in accordance with: • OTC medicines – Safety and efficacy data – new fixed combination medicines • Any other specific Australian or European Union (EU) guidelines relevant to the medicine, including the Guideline on Clinical Development of Fixed Combination Medicinal Products (CPMP/EWP/240/95 Rev1), adopted by the TGA.	6.f
Non-generic locally applied, locally acting medicine (e.g. topical medicine).	N5	5	Provide data in accordance with: • OTC medicines – Safety and efficacy data • Any other specific Australian or European Union (EU) guidelines relevant to the medicine, including the guideline Clinical requirements for locally applied, locally acting products containing known constituents (pp. 193–8 of Rules 1998 (3C) – 3CC12a).	6.g
Non-generic nicotine replacement therapy	N5	5	Provide data in accordance with: • the requirements detailed in the Guidelines on OTC applications for specific substances – Nicotine replacement therapy. • OTC medicines – Safety and efficacy data	6.h

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 requirement	Table reference number
Non-generic antiseptic	N5	5	Provide *in vitro* and *in vivo* data demonstrating the efficacy using the following suitable test methods (as relevant): • The *in vitro* test described in the FDA Tentative Final Monograph for first aid antiseptic products • The TGA disinfectant test (option D) for antiseptics modified to make it a quantitative method and supported by adequate validation data • The FDA Tentative Final Monograph for oral antiseptic drug products • FDA proposed monograph for antigingivitis /antiplaque drug products • The European Standard EN13727 for chemical disinfectants and antiseptics • FDA Tentative Final Monograph for health-care antiseptic drug products • The European Standard EN 1499 for hygienic handwashes • The European Standard EN 1500 for hygienic handrubs • The European standard EN 12791 for surgical hand disinfectants	6.i
Non-generic head lice treatment	N5	5	Provide data in accordance with: • Guidelines on OTC applications for specific substances – Head lice treatments. • OTC medicines – Safety and efficacy data	6.j
New active ingredient (new chemical entity)	N5	5	Provide data in accordance with all of the following: • Mandatory requirements for an effective application for prescription medicines • OTC medicines – Safety and efficacy data	6.k

Application type (more than one type may apply)	OTC Application level	CTD Module	Module 5 requirement	Table reference number
			• Any other specific Australian or European Union (EU) guidelines relevant to the medicine, including: – For topical medicines provide safety and efficacy data in accordance with the EU guidance *Clinical requirements for locally applied, locally acting products containing known constituents* (pp. 193–8 of Rules 1998 (3C) – 3CC12a). – For modified release medicines provide safety and efficacy data in accordance with the EU *Note for guidance on modified release and transdermal dosage forms: Section II (Pharmacokinetics and clinical evaluation)* (CPMP/EWP/280/96). – For fixed combination medicines or composite packs provide safety and efficacy data in accordance with the EU *Guideline on Clinical Development of Fixed Combination Medicinal Products* (CPMP/EWP/240/95 Rev1), adopted by the TGA.	

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	OTC medicines	Publication: 30 November 2015.
V1.1	Minor changes to clarify original publication and effective dates	Complementary and Over the counter Medicines Branch	1 March 2016
V1.2	Addition of footnote to Table 2: Module 3 - Quality	COMB	July 2021

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