Mandatory requirements and associated guidelines for new substance applications to vary the Permissible Ingredients Determination

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Presentation overview

1. Background
2. Overview of Mandatory Requirements and application process
3. Microorganism characterisation guidance
4. Australian Regulatory Guidelines for Sunscreens
5. COB guidance

Background:

Development of mandatory requirements

Regulatory framework for listed medicines

- All therapeutic goods included on ARTG
- Higher risk TG (based on ingredients and indications) ‘registered’. Full TGA evaluation of product.
- Lower risk (based on ingredients and indications) are ‘listed.
- Do not undergo pre-market evaluation of product. Safety and quality assured by other means e.g. evaluation of individual ingredients, GMP and sponsor self-certifications.

Approval of new ingredients for use in listed medicines

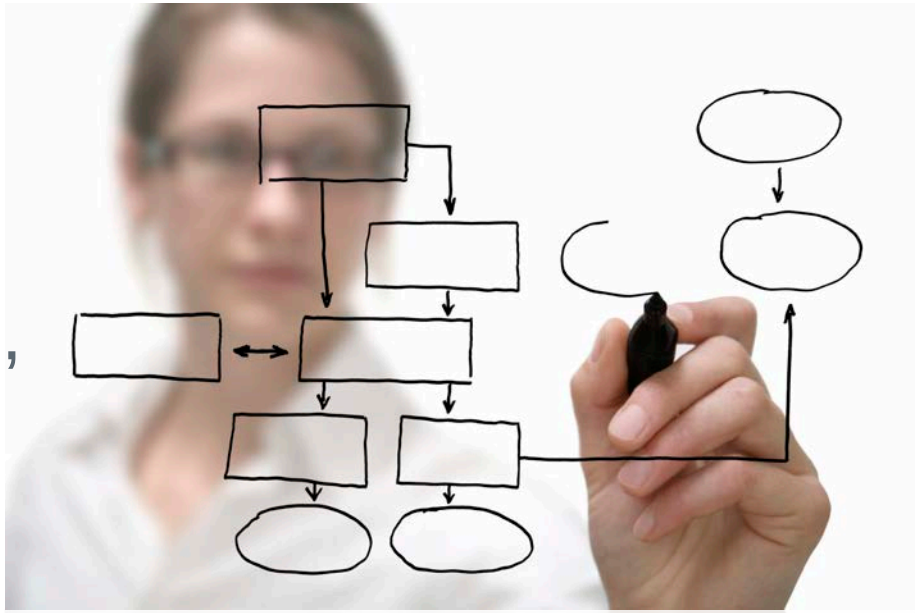
- Ingredients not currently permitted for listed medicines must be evaluated for Quality and Safety.
- Application required with supporting data.
- All approved ingredients included in the Permissible Ingredients Determination (s.26BB of the TG Act 1989).
- Ingredients can be used by other sponsors (unless market exclusivity provisions apply).

Review of Medicines and Medical Device Regulation

- 2016 MMDR review - recommendations accepted by Government:
  - Ingredients pre-market evaluated for safety and quality
  - Legislative timeframes for ingredient applications
  - Appeal rights
  - Defined applications and fee structure
  - COB pathway
  - Market exclusivity
- Public consultation late 2017 for business improvements required.

Development of mandatory requirements

- Extensive consultation through ComTech forum to develop ingredient application requirements from 2020-2023.
- Close attention to different types of ingredients (e.g. herbal vs microorganism, different routes of administration)
- Technical interlinked issues
- Holistic review needed: consistency, fit-for-purpose



Rationale for mandatory application requirements

- Mirrors other pre-market assessment processes (preliminary assessment).
- Ensures sufficient information is available for TGA to undertake a meaningful evaluation.
- Poor quality applications not unnecessarily evaluated.
- Greater transparency and predictability for applicants.
- Consistent standard when ingredients are accepted and evaluated.

- Prevents deficient applications from delaying evaluation of quality applications.
- More efficient evaluation that helps improve assessment timeframes.

Overview of the new application process

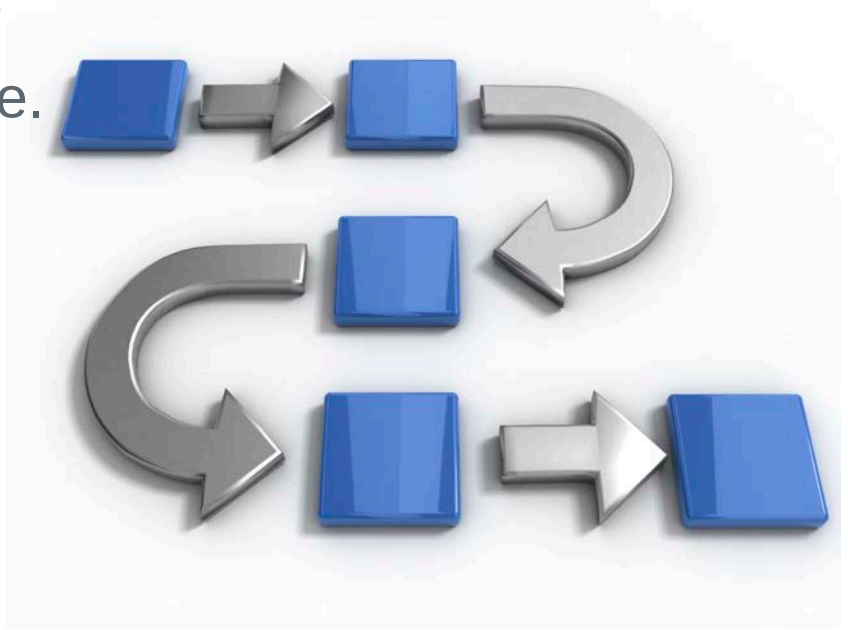
Mandatory requirements for an effective application to vary the Permissible Ingredients Determination

- **Effective for applications lodged from 1 February 2023**
  - Type of information required and how it is to be provided (e.g. folders named and structured corresponding to the relevant core information)
  - Table 1: administrative
    Table 2: information for quality (Monograph)
    Table 3: information for quality (non-monograph)
    Table 4: information for safety
- "Core information requirements" = data or justifications?
- Accompanying guidance 'Application requirements for new substances in listed medicines' – **"ARNS" – an update of previous guidelines.**

Overview of the application process for new ingredient or vary existing ingredient

Lodgement of application

- Complete form on TBS portal titled ‘Substance Evaluation,’ in the Applications menu under the heading Listed Medicine.
- Supporting data (dossier) attached to the application form (<100mb) or sent separately to the TGA via e-mail or using GovTeams.



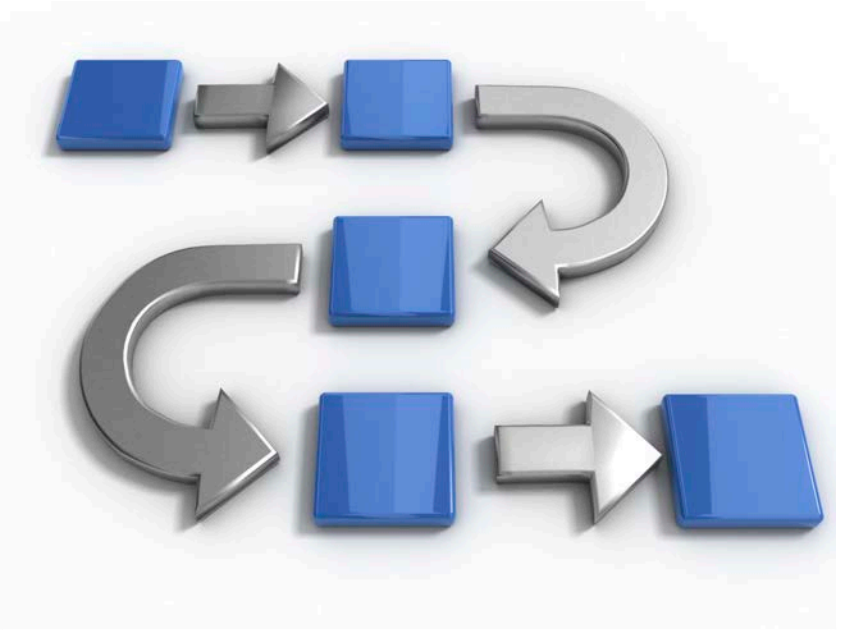
See:

- SECTION A – Application process for new substances for use as ingredients in listed medicines in the ARNS.
- User guide: Evaluation of substances for use in listed medicines and assessed listed medicines

Overview of the application process for new ingredient or vary existing ingredient

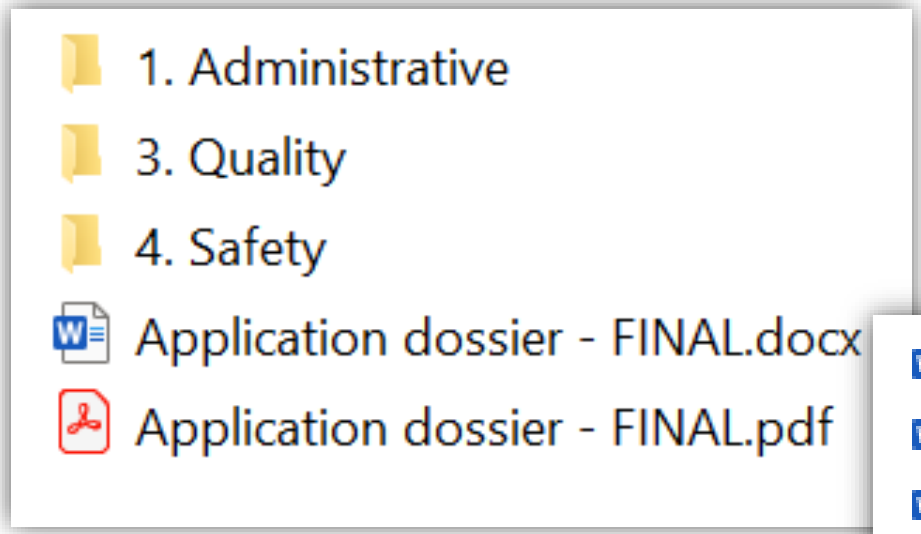
Preliminary assessment

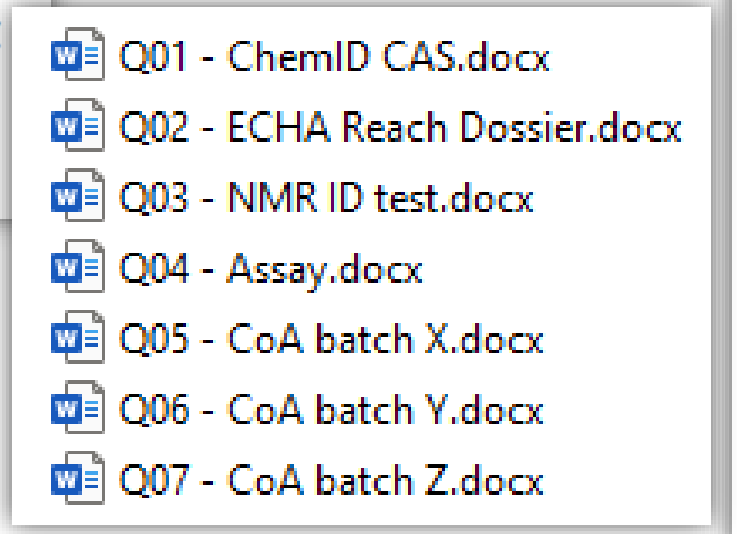
- TGA will undertake a preliminary assessment to ensure application form, fee, and information provided.
- Will assess if data/information or justification provided to address each core information requirement in Mandatory Requirements.
- Merits of justifications or data are not assessed during preliminary assessment.

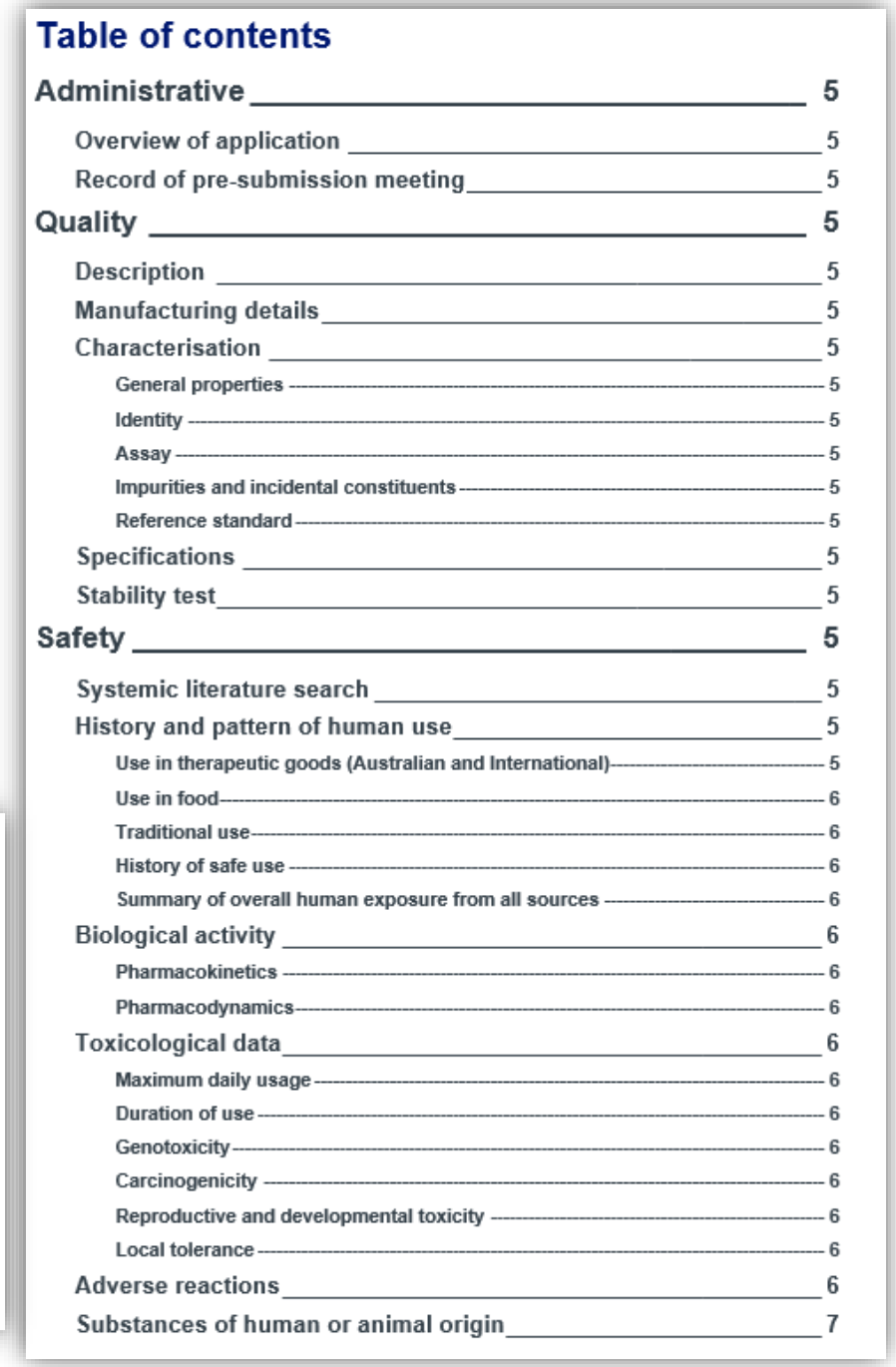


Overview of the application process

- Formatted in line with these headings by means of:
  - Organising the dossier
  - Folders containing references







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Evaluation

- If it passes notified in writing and invoice issued for the evaluation fee. Application will lapse if invoice not paid within two months.
- Merits of justifications or data assessed.
- TGA may request information during this phase.

Recommendation

- If Delegate considers the application can be approved with restrictions necessary to ensure safe use (e.g. warning statement for use in pregnancy, maximum daily dose), then may contact applicant to confirm agreement.

Changes to the newly developed data requirements

Quality

- For substances that are subject to a monograph in a default standard, reference to version number and name of current monograph as an option is acceptable.
- Manufacturer's details removed.
- Stratified the CG templates according to different types of substances:
  - Chemical entities/synthetic polymers
  - Herbal materials
  - Microorganisms
  - Substances of animal origin

Changes to the newly developed data requirements – cont'd

Safety

- Acute toxicity studies not required.
- Flexibility for data requirements (animal/human/in vitro studies, history of use) to address Toxicology.
- Guidance for specific types of substances (e.g. microorganisms vs herbal materials).
- New guidance for dermal substances.

Summary of requirements

- See Table 3 (in Appendix) in ARNS for a summary of requirements for different ingredients.

Core information requirement		Substances for oral use[3]	Micro-organisms[4]	Dermal active substances[5]	Dermal excipient substances[5]
QUALITY					
Description	Description of the substance	✓	✓	✓	✓
SAFETY					
Systematic literature search	A systematic literature search on the substance; with the search strategy and results with justification for inclusion/exclusion of data	✓	✓	✓	✓

New guidance: Requirements for microorganism characterisation

Newly developed guidance requirements for microorganism characterisation

- Relates to applications for new microorganism strains and responds to requests for clarity on TGA expectations.
- Consulted extensively with stakeholders to develop guidance: ComTech, FSANZ, ACCESS, ASM, ACCM
- Reviewed international approaches e.g. FAO WHO, EFSA, HC, IPA, ISAPP.

- The guidance bridges a significant gap in current application guidelines and ensures that microorganisms, when identified and characterised, are safe for their intended use.

Newly developed guidance requirements for microorganism characterisation

- Specifies data requirements for the premarket assessment of new live and whole/intact non-viable microorganisms.
- The headings of each core information requirement correspond with the headings in the Mandatory requirements and ARNS.
- Should be read in conjunction with ARNS.
- Guidance on establishing strain equivalence if leveraging data from a different strain.

Updates to the Australian Regulatory Guidelines for Sunscreens

Update to the ARGS

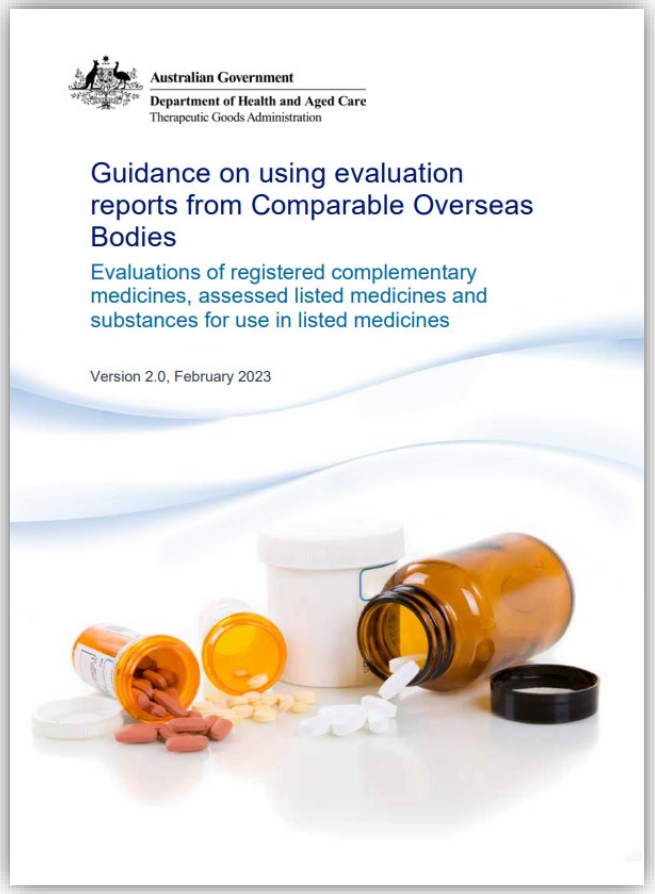
- Updated to align with requirements for new dermal substances for use in listed medicines.
- Headings of each core information requirement in ARGS correspond with headings in the ARNS.
- Applicants to follow V3.0 ARGS for guidance on new applications for ingredients for use in listed therapeutic sunscreens from 9 May 2023.

Updates regarding use of evaluation reports from Comparable Overseas Bodies

Use of evaluation reports from Comparable Overseas Bodies

- Updated COB guidance published in February 2023 – significant changes to guidance to improve readability and clarity following industry feedback.
- Revised list of approved COBs (e.g. SCCS)
- Updated references to IN1 application category to align with new Regulations – application based on a COB report for safety, and quality based on a default standard.

Requirements for an application utilising the COB-based process



Provide:

- A completed COB report-based process – Substance evaluation checklist for each COB report provided;
- A full un-redacted English copy of the COB evaluation report(s); and
- Gap analysis for COB report.

Gap analysis

1. **Discuss how COB report addresses the mandatory requirements for safety/quality for the application (recommend to use a table)**

Core Requirements	Location in [redacted] COB Report
Table 3 Requirements – Information to Demonstrate Quality	
Description	Section 3.1 (pg. 5)
Manufacturing details	Section 3.3 (pg. 6)

2. **Any new data since COB report was approved (updated literature search, new tox/clinical studies, new adverse event reports)**

Expected to only be needed regarding safety e.g. updated literature search, updated adverse events, new tox/clinical studies.

Therapeutic Goods Administration (TGA)

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Website references

TGA website	www.tga.gov.au
Mandatory requirements for an effective application to vary the Permissible Ingredients Determination	https://www.tga.gov.au/resources/resource/guidance/mandatory-requirements-effective-application-vary-permissible-ingredients-determination
Application requirements for new substances in listed medicines (ARNS)	https://www.tga.gov.au/resources/resource/guidance/application-requirements-new-substances-listed-medicines
User guide: Evaluation of substances for use in listed medicines and assessed listed medicines	https://www.tga.gov.au/resources/resource/guidance/user-guide-evaluation-substances-use-listed-medicines-and-assessed-listed-medicines
Overview of Compositional Guidelines and templates	https://www.tga.gov.au/resources/resource/guidance/overview-compositional-guidelines-and-templates

Questions?

www.tga.gov.au

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration