



Australian Government
Department of Health
Therapeutic Goods Administration

Guidance on using evaluation reports from Comparable Overseas Bodies

Evaluations of registered complementary medicines, assessed listed medicines and substances for use in listed medicines

Version 1.1, April 2022

TGA Health Safety
Regulation



Copyright

© Commonwealth of Australia 2022

This work is copyright. You may reproduce the whole or part of this work in unaltered form for your own personal use or, if you are part of an organisation, for internal use within your organisation, but only if you or your organisation do not use the reproduction for any commercial purpose and retain this copyright notice and all disclaimer notices as part of that reproduction. Apart from rights to use as permitted by the *Copyright Act 1968* or allowed by this copyright notice, all other rights are reserved and you are not allowed to reproduce the whole or any part of this work in any way (electronic or otherwise) without first being given specific written permission from the Commonwealth to do so. Requests and inquiries concerning reproduction and rights are to be sent to the TGA Copyright Officer, Therapeutic Goods Administration, PO Box 100, Woden ACT 2606 or emailed to tga.copyright@tga.gov.au.

Contents

Guidance on using evaluation reports from Comparable Overseas Bodies	1
Scope of guidance document	4
Overview of the COB report-based process	4
Purpose of COB report-based process	4
Challenges in identifying suitable COB reports	4
Application framework	5
Overview of the COB-based process	6
Criteria for identifying COBs and accepting reports	7
Stage 1: Establishing similarity between the body and the TGA	7
Stage 2: Criteria for acceptance of COB evaluation reports	9
List of COBs for registered complementary medicines, assessed listed medicines and substances for use in listed medicines	13
Submission requirements for the COB report-based process	18
Registered complementary medicines and assessed listed medicines	18
Substances for use in listed medicines	18

Scope of guidance document

Where possible, the TGA uses evaluation reports from comparable overseas bodies (COBs) in the evaluation of applications for registered complementary medicines, assessed listed medicines and substances for use as ingredients in listed medicines.

This guidance provides:

- an overview of the COB report-based process and application categories
- criteria for the TGA's identification of COBs and acceptance of COB evaluations
- the list of current COBs
- submission requirements for the use of COB evaluation reports.

Overview of the COB report-based process

Purpose of COB report-based process

The COB report-based process is available for:

- applications for registered complementary medicines
- applications for assessed listed medicines
- applications for evaluation of a substance for use as an ingredient in listed medicines.

The COB report-based process allows technical evaluation reports from identified bodies to be used by TGA to assess applications against the Australian requirements.

The aim of the process is to:

- encourage harmonisation and sharing of knowledge
- reduce TGA duplication of evaluations undertaken by COBs, while still maintaining existing quality, safety and efficacy standards for medicines supplied in Australia
- allow applications following the [Application framework](#) to have shorter evaluation timeframes.

Challenges in identifying suitable COB reports

Given the nature of complementary medicines and other low-risk medicinal products, few international bodies evaluate the quality, safety and efficacy of substances or medicines in a single report. Challenges that we face in identifying and using COB reports include, but are not limited to:

- differences in evaluation processes: complementary and other low-risk medicinal substances or products may be regulated internationally as foods, medicines, cosmetics or dietary supplements
- differences in inter-agency decisions: assessing these products or substances against different evaluation processes may lead to differences in inter-agency decisions about quality, safety and efficacy

- difficulties accessing un-redacted or unpublished evaluation reports
- use of a product or substance in the Australian context may differ from how it is used internationally
- language barriers.



Due to these challenges, the TGA makes the final regulatory decision on applications to ensure that safety, quality and/or efficacy are established in line with the Australian regulatory framework.

Application framework

The following application categorisation framework allows us to undertake evaluations based on a combination of data independently evaluated by the TGA and reports from COBs:

- L(A)1 – L(A)3 for assessed listed medicines
- IN1 – IN4 for substances for use as ingredients in listed medicines
- RCM1 – RCM5 for registered complementary medicines.

Under the application categorisation framework, applications in each category may be evaluated in one of three ways:

1. Evaluation based solely on the use of COB reports

Applicants provide evaluation report(s) and a complete data dossier for the same substance or medicine from a COB that meets all minimum data requirements for safety, quality and/or efficacy (L(A)2, IN1 and RCM2). Safety reports or quality reports from one COB may also be submitted through the IN1 application category in conjunction with a suitable quality/safety report from another COB.

2. Mixed evaluation

Applicants provide a combination of COB report(s) that meet minimum data requirements for safety, quality, and/or efficacy in combination with minimum data requirements for an independent evaluation of the missing parameters by the TGA (IN2, IN3, RCM3 and RCM4).

3. Full independent evaluation

All quality, safety, and/or efficacy parameters independently evaluated by the TGA (L(A)3, IN4 and RCM5).

Applications accepted for evaluation through the COB report-based process are expected to have shortened evaluation and decision timeframes when compared to the standard evaluation/assessment processes.



The following guidance for each application type sets out the information and corresponding forms and checklists required to be submitted in an application:

- [Assessed listed medicines evidence guidelines](#) for applications for an assessed listed medicine
- [ARGCM Part C: New substance evaluation](#) for applicants proposing a

substance for use in listed medicines

- [ARGCM Part D: Registered complementary medicines](#) for applications for a new registered complementary medicine.

Overview of the COB-based process

- The COB process has been divided into 2 stages: criteria for identifying COBs (Stage 1) and criteria for accepting COB reports (Stage 2). Below is an overview of how the COBs included in the [List of bodies or jurisdictions determined to be COBs for complementary and listed medicines](#) were identified by TGA.
- Applicants can then use the Stage 2 [Criteria for identifying COBs and accepting reports](#) to determine if a particular COB evaluation report is suitable for a particular application. COB reports can then be included in an application along with the full submission dossier. See [Submission requirements for COB reports](#) for more information.
- During application screening, the TGA will confirm whether the application is eligible for the COB report-based process and that the correct application category has been selected.
- Depending on the quality and scope of the COB evaluation report(s) provided to the TGA, the TGA will not re-evaluate the data provided in the dossier that has been previously evaluated and approved by a COB. Where an applicant provides COB report(s) that meet all minimum data requirements, the TGA will only need to evaluate data generated specifically for the Australian context (for example: Australian labels or storage conditions). However, if any issues arise during TGA's review of the COB assessment report, the TGA will review the data provided in the dossier. In some instances, additional data may need to be considered (for example, to address data gaps or additional safety data generated since the COB evaluation report approval).

It is the responsibility of the applicant to:

- obtain any relevant un-redacted COB evaluation reports, in English
- provide a justification for how the content of the COB evaluation report(s) meet the TGA's technical requirements, for example: the ARGCM, assessed listed medicines evidence guidelines and any other relevant technical regulatory guidelines
- undertake a gap analysis to address data gaps due to insufficient data
- undertake a gap analysis to account for any new information generated since the COB evaluation report was approved.

Where the submission requirements for COB reports are not met, the application must be resubmitted for independent evaluation through the appropriate application category.



Pre-submission meetings

Due to differences in regulatory frameworks and evaluation process requirements, some applications may not be suited to the COB report-based process. We recommend that applicants request a pre-submission meeting with TGA to discuss their application before lodging.



The TGA will also accept evaluation reports from overseas bodies that are not included on the list of TGA-approved COBs as part of a full independent evaluation by the TGA (for example: IN4, L(A)3 and RCM5), provided the [Stage 2 Criteria](#) for accepting COB evaluation reports are met.

Criteria for identifying COBs and accepting reports

The TGA has a set of criteria to identify (1) suitable COBs and (2) COB evaluation reports using best-practice evaluation processes that best align with the TGA's regulatory framework to an acceptable level.

The criteria are applied in two stages:

- [Stage 1 - Criteria for identifying COBs](#)
- [Stage 2 – Criteria for accepting COB reports](#)



Note that we will consider accepting reports from COBs that may not meet all the criteria where the applicant can provide adequate justification and/or additional data as required.

Stage 1: Establishing similarity between the body and the TGA

The first stage explains the criteria applied to establish sufficient similarity between the overseas body and the TGA. This process enabled the TGA to identify suitable bodies for the COB report-based process. These COBs were then included in the [List of bodies or jurisdictions determined to be COBs for complementary and listed medicines](#). Reports from these COBs can then be used to support an application submitted through a COB report-based process, provided the evaluation report(s) also meets the Stage 2 criteria.

Stage 1 criterion 1

The COB is an internationally recognised body with an established track record of evaluating similar food, chemical or medicinal products/substances.

To meet this criterion, the COB:

- Has a similar evaluation process to the TGA in terms of what must and must not be taken into account when making decisions.
- Conducts:
 - independent *de novo* pre-market evaluations of the type of applications that are of interest to us (for example, evaluations of plant or herbal materials, vitamins and minerals)
 - similar pre-market safety, quality and efficacy evaluations of substances and/or medicines

- similar post-market activities including pharmacovigilance programs.

Stage 1 criterion 2

The COB has a transparent system for decision-making.

Noting the uniqueness of the Australian complementary and listed medicines regulatory framework, this criterion does not limit the contexts or frameworks from which we will accept evaluation reports. Instead, it requires that the TGA be able to develop confidence in the transparency and robustness of the operating principles of the COB.

To meet this criterion, the COB would need to:

- Have a transparent system for its evaluation processes.
- Have a transparent system for legal accountability including:
 - confidentiality
 - intellectual property
 - impartiality
 - transparency
 - conflict of interest processes.
- Have a clear decision-making framework.
- Have clear risk-assessment methodologies that do not conflict with our operating principles.

Stage 1 criterion 3

The COB uses international guidelines and standards consistent with those adopted by the TGA.

Rather than mandating specific guidelines, this criterion captures the principle that we need to have confidence in the scientific processes used. To best make use of overseas evaluations, any differences in how these international standards are adopted needs to be well understood.

To meet this criterion, the COB would need to:

- Have established scientific evaluation processes, such as processes in accordance with:
 - pharmacopoeial standards adopted by Australia:
 - § *European Pharmacopoeia*
 - § *British Pharmacopoeia*
 - § *United States Pharmacopoeia – National Formulary*
 - the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) or other international guidelines.

Stage 1 criterion 4

The TGA should have, or be able to establish, a relationship with the COB.

To meet this criterion, the COB would need to:

- Be able to conduct their business and release reports in English.
- Give Australian applicants the evaluation reports in English for inclusion in the Australian application (this can include reports that have been translated into English from another language by the COB, or a certified translation provided by the applicant). Obtaining a certified translation is not the responsibility of the TGA.
- Be able to interact with the TGA in English, particularly where a sponsor submits certified English translations of evaluations.
- Be able to clarify information and address issues of confidentiality or data protection with the TGA if required.

Stage 2: Criteria for acceptance of COB evaluation reports

Stage 2 criteria focus on the specifics of a particular application. The following criteria will be applied to determine whether a COB report provided by an applicant is suitable for the particular application and therefore can be used to support the application.



The TGA reserves the right to require the applicant to resubmit their application under a different application category if the COB report provided by the applicant does not meet the Stage 2 criteria.

Stage 2 criterion 1

The substance or medicine described in the COB report should be equivalent to that proposed in the application.

Any differences in characteristics such as formulation, manufacture, and indications must be clearly justified by the applicant. To meet this criterion:

- The evaluation report should relate to the same medicine or substance as approved by or submitted to the COB, and have the same:
 - formulation
 - quality aspects
 - dosage form
 - dose
 - directions for use
 - route of administration.
- The manufacturing process should be comparable to that evaluated by the COB. Under certain conditions, additional manufacturing sites can be included in the application to the TGA, where that manufacturing site has been validated and shown to be the same or better than the original manufacturer.
- The proposed indication(s) for the medicine should be based on similar:
 - population demographics
 - disease profiles

- expectations regarding public health outcomes between Australia and the COB.

There should be no new indications proposed beyond what the report considered.

For generic products, the proposed indication(s) should be the same as the indication(s) approved for the originator. For non-generic products, acceptable differences between the COB-approved and proposed indication(s) are limited to minor changes in the wording or minor differences in expression, as long as the text describes the same:

- dosing range
- patient population
- health outcome expectation
- intent and meaning.



Inter-agency comparison of efficacy is a complex process due to the different levels of indications/claims allowed and evidence required by each body.

The evidence requirements may be comparable in some situations; however, in other circumstances this will not be the case. In these circumstances, **the TGA will make the final regulatory decision** ensuring that efficacy is established in line with the Australian regulatory framework.

Stage 2 criterion 2

Evaluation reports should be prepared using guidelines and standards consistent with those used by the TGA.

To meet this criterion:

- Evaluation reports should be consistent with the methodology used by the TGA, for example they should contain information consistent with the Common Technical Document (CTD) requirements.
- Evaluation reports should contain all information necessary to support the relevant assessment parameters (safety, quality and/or efficacy).



Differences in methodology do not necessarily prevent the use of evaluation reports. However, applicants should address any differences by providing:

- additional information to address any data gaps or other concerns
- a justification explaining how the content of the COB report meets TGA's technical requirements.

The absence of this information may mean that the application cannot be accepted through the COB report-based process.

Stage 2 criterion 3

Evaluation reports should be un-redacted and complete.

To meet this criterion, the complete reports should include correspondence related to the application (for example, questions asked of, and deliberations by advisory bodies). The Australian applicant is responsible for providing the reports to us when lodging the application.

Stage 2 criterion 4

The TGA should be able to use reports from COBs and any supplementary information to publish general information about the safety, quality and/or efficacy of the medicine.

To meet this criterion, reports that are provided to us should not be subject to any restrictions on use or disclosure by the TGA beyond what would normally apply with any application.

For more information, see:

- [TGA approach to disclosure of commercially confidential information \(CCI\)](#).

Stage 2 criterion 5

The report should be an independent evaluation made by a COB.

To meet this criterion:

- The submitted report should be fully written by the COB (a *de novo* report).
- The submitted report should present an independent evaluation of the data provided to the COB and not be an acceptance of another body's marketing approval.



Reports drafted as part of a self-affirmed/self-assessed report, for example: the Generally Recognized as Safe (GRAS) self-affirmation, are not suitable as an independent *de novo* evaluation.

Stage 2 criterion 6

Where the COB makes decisions relating to market approval, the following 2 criteria are required:

a. The medicine should have received full overseas marketing approval following the evaluation of the application by the COB.

To meet this criterion:

- The medicine approved by the COB should be equivalent to the medicine proposed in the application (refer to Criterion 1).
- The medicine should not be subject to any further restrictions or conditions that have not been identified in the report.
- The medicine should not have resulted in a delayed, deferred, rejected, refused, cancelled or withdrawn application or marketing approval at any time, in any country, i.e. the medicine must have a current overseas marketing approval (unless otherwise justified).

b. The substance should have received approval for use following the evaluation of the application by the COB.

To meet this criterion:

- The substance approved by the COB should be equivalent to the substance proposed in the application (refer to Criterion 1).
- The substance should not be subject to any further restrictions or conditions that have not been identified in the report.
- The substance should not have resulted in a delayed, deferred, rejected, refused, cancelled or withdrawn application at any time, in any country, i.e. the substance must have a current overseas approval (unless otherwise justified).

List of COBs for registered complementary medicines, assessed listed medicines and substances for use in listed medicines

The TGA will consider evaluation reports from the bodies specified in Table 1 (below) for use in the COB report-based process. This list has been determined by the Secretary for the purposes of regulation 16GJ of the Therapeutic Goods Regulations 1990.

The TGA will continue to engage with overseas bodies to expand and refine this list.



Some products regulated as complementary medicines in Australia are evaluated as prescription medicines overseas. These products are assessed against more stringent safety/quality/efficacy requirements than Australian listed complementary medicinal products. Therefore, the TGA will accept COB reports for complementary medicinal products that have been evaluated as prescription medicines by the COBs listed in Table 1 where the regulatory pathway has required a full data package/complete data dossier for assessment.

Table 1: List of bodies or jurisdictions determined to be Comparable Overseas Bodies (COBs) for registered complementary medicines, assessed listed medicines and substances for use in listed medicines

Body	Country or jurisdiction	How evaluation reports can be used			Notes
		Safety	Quality	Efficacy	
Australian Industrial Chemicals Introduction Scheme (formerly NICNAS)	Australia	ü	û	û	Reports may be used to support safety of substances proposed for use as ingredients in listed medicines (IN1 or IN2) when the substance is intended to be used as an excipient ingredient in sunscreens or other topical products.
Cosmetic Ingredient Review (CIR)	United States	ü	û	û	Reports may be used to support safety of substances proposed for use as ingredients in listed medicines (IN1 or IN2) when the substance is intended to be used as an excipient ingredient in sunscreens or other topical products.

Body	Country or jurisdiction	How evaluation reports can be used			
		Safety	Quality	Efficacy	Notes
European Food Safety Authority (EFSA)	European Union	ü	ü	û	Reports may be used to support safety and quality of substances proposed for use as ingredients in listed medicines (IN1, IN2 or IN3) when the substance is intended for oral use.
European Medicines Agency (EMA)	European Union	ü	û	û	EU monographs may be used to support safety of substances proposed for use as ingredients in listed medicines (IN1 or IN2) when the substance is a herbal ingredient.
		ü	ü	ü	Reports for medicines submitted under Article 8(3) of Directive 2001/83/EC (full or full-mixed application, complete dossier) and assessed via the centralised procedure ¹ may be used to support safety, quality and efficacy of registered complementary medicines (RCM2, RCM3 or RCM4) and efficacy of assessed listed medicines (L(A)2).
Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER)	United States	ü	ü	ü	Reports that form part of a New Drug Application may be used to support the safety, quality and efficacy of registered complementary medicines (RCM2, RCM3 or RCM4); safety and quality of substances for use as ingredients in listed medicines (IN1, IN2 or IN3); and efficacy of assessed listed medicines (L(A)2).

¹ See <https://www.ema.europa.eu/en/about-us/what-we-do/authorisation-medicines#centralised-authorisation-procedure-section> for information about the types of medicines that can be evaluated under the centralised procedure.

Body	Country or jurisdiction	How evaluation reports can be used			
		Safety	Quality	Efficacy	Notes
		ü	ü	û	Monographs for OTC ingredients determined to be 'Generally Recognized as Safe and Effective (GRASE)' may be used to support the safety and quality ² of substances proposed for use as ingredients in listed medicines (IN1, IN2 or IN3)
Food Standards Australia New Zealand (FSANZ)	Australia	ü	û	û	Reports may be used to support the safety of substances proposed for use as ingredients in listed medicines (IN1 or IN2) when the substance is intended for oral use.
Health Canada (HC)	Canada	ü	û	û	Reports for Natural Health Products may be used to support safety of substances proposed for use as ingredients in listed medicines (IN1, IN2 or IN3).
		û	û	ü	Reports for Natural Health Products may be used to support efficacy ³ of assessed listed medicines [L(A)2].
		ü	û	ü	Reports for Natural Health Products may be used to support safety and efficacy ⁴ of registered complementary medicines (RCM2, RCM3 or RCM4).

² Stability of the ingredient will be considered separately in accordance with ICH requirements as this parameter is not covered by FDA monographs

³ Health Canada reports to support efficacy must rely primarily on clinical trial reports, systematic reviews and meta-analyses to support the indications.

⁴ Health Canada reports to support efficacy must rely primarily on clinical trial reports, systematic reviews and meta-analyses to support the indications.

Body	Country or jurisdiction	How evaluation reports can be used			
		Safety	Quality	Efficacy	Notes
		ü	ü	û	Monographs ⁵ from the Compendium of monographs may be used to support the safety and quality of substances proposed for use as ingredients in listed medicines (IN1, IN2 or IN3).
Health Sciences Authority (HSA)	Singapore	ü	û	û	Reports for existing ingredients used in Chinese Proprietary medicines with a proposed new scope for use (eg: dose, therapeutic use, route of administration) or with emerging safety concerns may be used to support safety of substances proposed for use as ingredients in listed medicines (IN1 or IN2).
Joint FAO/WHO Expert Committee on Food Additives (JECFA)	Global	ü	û	û	The WHO Technical Report Series and WHO Food Additives series (FAS) may be used to support safety of substances proposed for use as ingredients in listed medicines (IN1 or IN2) when the substance is intended for oral use.
		û	ü	û	The FAO JECFA Monographs ⁶ may be used to support quality of substances proposed for use as ingredients in listed medicines (IN1 or IN3) when the substance is intended for oral use.

⁵ Stability of an ingredient will be considered separately in accordance with ICH requirements irrespective of the presence of a monograph as this testing parameter is not included in monographs.

⁶ Stability of an ingredient will have to be considered separately in accordance with ICH requirements irrespective of the presence of a monograph as this testing parameter is not included in monographs.

Body	Country or jurisdiction	How evaluation reports can be used			
		Safety	Quality	Efficacy	Notes
Pharmaceutical and Medical Devices Agency (PMDA)	Japan	ü	ü	û	Reports for Category 1 quasi drugs and Category 1 OTC products (herbal medicines) may be used to support the safety and quality of registered complementary medicines (RCM3) .
Scientific Committee on Consumer Safety (SCCS)	European Union	ü	û	û	Reports may be used to support safety of substances proposed for use as ingredients in listed medicines (IN1 or IN2) when the substance will be assessed as an excipient ingredient in sunscreens or other topical products.

Submission requirements for the COB report-based process

The information below provides guidance on the submission requirements for the COB report-based process.

Registered complementary medicines and assessed listed medicines

For the COB report-based process, applicants must submit the complete dossier that was submitted to the COB with an Australian-specific Module 1, including:

- In Module 1.2, the relevant completed COB application checklist:
 - COB report-based process – checklist for registered complementary medicines
 - COB report-based process – checklist for assessed listed medicines

This checklist is mandatory for COB report-based applications and helps the applicant and TGA identify whether the application meets the requirements for the selected application pathway.
- For generic medicines, in Module 1.2.1, : evidence that the reference product used in any evaluation of bioequivalence is identical to the Australian reference product (see [Guidance 15: Biopharmaceutic studies](#)).
- In Module 1.11.1, full details of whether the application has been approved, deferred, withdrawn, rejected, cancelled, approved on appeal, delayed or received a 'refusal to approve' in another jurisdiction.
- In Module 1.11.4, the complete and un-redacted set of final COB evaluation reports, in English.
- In Module 1.11.4, thorough justification of how the COB report meets TGA technical requirements and a gap analysis if required.

Substances for use in listed medicines

For the COB report-based process, applicants must submit the complete dossier that was submitted to the COB with [Administrative information](#) and [General substance information](#) as described in [ARGCM Part C: New substance evaluation](#), including:

- The completed COB report-based process – Substance evaluations checklist. This checklist is mandatory for COB report-based applications and helps the applicant and TGA identify whether the application meets the requirements for the selected application pathway.
- Full details of whether the application has been approved, deferred, withdrawn, rejected, cancelled, approved on appeal, delayed or received a 'refusal to approve' in another jurisdiction. This requirement seeks to capture complicated or contentious applications that require a deeper consideration of the data in the Australian context.
- The complete and un-redacted set of final COB evaluation reports, in English.

- Thorough justification of how the COB report is applicable to use in the Australian context. There may be components of decisions made by COBs that may not be appropriate or relevant in Australia, or may not be able to be automatically applied to uses in Australia. This may apply to:
 - substances evaluated by a COB as a food, dietary supplement or cosmetic
 - situations where Australian conditions of use must be taken into consideration, for example: substances intended for use in sunscreens may be subject to different exposure level test limits in different jurisdictions.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Complementary and Over the Counter Medicines Branch	November 2019
V1.1	<p>Amendments to the List of COBs including:</p> <ul style="list-style-type: none"> • Removal of '<i>European Pharmacopoeia</i> monographs' • Updated NICNAS to Australian Industrial Chemicals Introduction Scheme (formerly NICNAS) <p>Minor amendments to document including:</p> <ul style="list-style-type: none"> • Removal of the mention of default standards as these are not within the scope of this document • Typographical errors 	Complementary and Over the Counter Medicines Branch	April 2022

Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia

Email: info@tga.gov.au Phone: 1800 020 653 Fax: 02 6203 1605

<https://www.tga.gov.au>

Reference/Publication # D22-5389104