Australian Government
Department of Health
Therapeutic Goods Administration

Comparable overseas regulators (CORs) for prescription medicines

Criteria for COR report-based process

Version 1.2, October 2019

TGA Health Safety Regulation

Contents

The TGA makes use of assessments from comparable overseas regulators (CORs), where possible, in the regulation of prescription medicines.

In response to the Medicines and Medical Devices Review (MMDR) we have implemented:

- transparent criteria for identifying CORs and
- a process for use of overseas reports.

Criteria for identifying CORs

These criteria help identify opportunities for enhanced international collaboration in the regulation of prescription medicines.

These criteria apply to the COR report-based processes.

The COR criteria are applied in two stages:

- Stage 1: The first stage sets out the preliminary criteria that confirm that there is sufficient similarity between TGA and the overseas agency to support collaborative work by the TGA's use of an existing, complete assessment report.
- Stage 2: The second stage outlines the parameters that are relevant to a particular submission. These would be considered at the time a submission is made to TGA that proposes reliance on COR assessment reports instead of *de novo* evaluation. These criteria can also inform first stage considerations.

These criteria have been applied to generate an initial list of overseas agencies for the COR report-based process.

Stage 1 criteria

The first stage sets out the preliminary criteria that confirm that there is sufficient similarity between the overseas agency and us to support collaborative work of this nature.

Criterion 1

The COR's regulatory framework should be similar to that of TGA in terms of what must and must not be taken into account in making regulatory decisions.

To meet this criterion the COR would need to:

- conduct similar pre- and post-market regulatory activities, including
  - Good Manufacturing Practice inspections programs
  - pharmacovigilance programs
  - full *de novo* assessments (safety, quality and efficacy) of the type of applications that are of interest to us (e.g. assessments of new chemical or biological entities, generic medicines, biosimilars and subsequent variations to these goods)
- have a transparent system for regulating therapeutic goods, including its assessment processes and legal accountability (conflict of interest processes).

Criterion 2

The TGA must have established a formal and robust framework for cooperation with the COR.

To meet this criterion the COR would need to have an agreed Memorandum of Understanding (MOU) or exchange of letters with the TGA that allows clear, open, secure communication on regulatory issues and transmission of confidential information.

Criterion 3

The COR must use international guidelines and standards consistent with those adopted by the TGA.

To meet this criterion the COR would need to have established scientific evaluation processes in accordance with The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and other international guidelines, as well as pharmacopoeial standards adopted by Australia (the European Pharmacopoeia, British Pharmacopoeia and United States Pharmacopeia).

To best make use of overseas assessments, any differences in how these international standards are adopted will need to be well understood.

At the application level, when there are differences identified in the adoption of technical guidelines between the COR and TGA that are relevant to a particular application, this criterion may not be met.

Criterion 4

The COR should be able to conduct their business and release reports in English.

The applicant must have access to the assessment reports and associated supporting documentation (such as (but not limited to) committee/advisory bodies minutes) in English for inclusion in the Australian application (this can include reports that have been translated into English from another language by the COR).

Stage 2 criteria

Stage 2 criteria focus on the specifics of a particular application. Once an overseas regulator has been identified as a source of assessment reports, the following considerations will be applied to determine whether the proposed use of COR reports can proceed.

Criterion 5

Equivalent indication is proposed for the medicine (including dosage regimen and route of administration).

To meet this criterion:

- the proposed indication for the medicine would need to be based on broadly similar population demographics, disease profiles, and expectations regarding public health outcomes between Australia and the COR
- any differences would need to be identified and justified by the applicant
- the medicine application in Australia is identical to the COR application, that is, the Australian medicine application is not a subset or otherwise modified application of the COR application.

Criterion 6

The medicine for which Australian registration is sought is singular and identical to that approved by, or submitted to, the COR (i.e. dosage form, strength, formulation and manufacture).

To meet this criterion, the assessment reports must relate to the same medicine (identical in terms of quality aspects of the product) and each Australian medicine registration application relates to a single medicine and ARTG entry.

The manufacturing process must be identical to that assessed by the COR but additional manufacturing sites can be included in the application to the TGA (under certain conditions).

Criterion 7

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

To meet this criterion, the assessment reports should be prepared in the Common Technical Document (CTD) format and consistent with a methodology used by the TGA. A key consideration is whether the assessment reports have the required scope. For example, in the case of clinical assessments, the TGA would consider what studies and analyses have been included, and for each of these, the data cut-off for analysis.

Differences in methodology may not prevent the use of the assessment reports. However, the TGA would require additional information to address any gaps or concerns, reducing the benefit of using an overseas report. Please also note that if any other assessments of an application by COR have led to differences in indications or patient groups being approved, then this rationale will need to be provided, along with all associated assessment reports and this complexity should be discussed with the TGA prior to submission.

Criterion 8

Assessment reports must be un-redacted and complete.

To meet this criterion, the complete reports should include correspondence related to the application (e.g. questions asked of, and deliberations by, advisory bodies).

The Australian applicant is responsible for providing the reports to us when lodging the application.

Criterion 9

The TGA should be able to use assessment reports and any supplementary information generated during the evaluation process as part of Australian Public Assessment Reports (AusPARs).

To meet this criterion, reports that are provided to the TGA should not be subject to any restrictions on use or disclosure by the TGA other than those which would apply to any material provided in an application dossier (e.g. these reports must be able to be used as the basis for published AusPARs).

COR report-based process

The COR report-based process is open to prescription medicines registration applications, where the medicine has received full overseas marketing approval following a *de novo* evaluation.

Applications can relate to all types of new prescription medicines, including new chemical entities, new fixed dose combinations, generic medicines, biological medicines and biosimilars.

This process can also be used for variations to existing medicines, including extension of indications or new dosage forms and changes to product information documents that would normally require evaluation of clinical data.

Importantly, the application must not have been delayed, deferred, rejected, refused or withdrawn at any time, in any country.

A COR report of a literature-based submission is unlikely to be suitable for the COR process as the search strategy and evidence may be rapidly superseded. Further consideration will also need to be given to the different methodology used by different jurisdictions for literature-based submissions, and hence further justifications may be required.

Applicants can use the COR criteria to identify suitable assessment reports that have been obtained from a COR. These reports can then be included in a COR report-based application along with the dossier that was submitted to the COR and an Australian Module 1.

- List of countries/jurisdictions for the COR report-based process
- Submission requirements
- Timeframes and milestones
- Requirements for indications

Depending on the quality and scope of the overseas assessment package provided to the TGA, the need to evaluate the data within the dossier may be reduced to a greater or lesser degree.

Pre-submission meeting is encouraged

Due to differences in regulatory frameworks and process requirements, there may be certain applications that are not suited for the COR report-based processes (for example, medicines that include a medical device component).

All applications must meet existing Australian requirements, including those based on COR reports.

We highly recommend that applicants request a pre-submission meeting with TGA to discuss their application before lodging.

Related information

- Application forms for this process are available at Prescription medicines application forms.

Contact streamlinedsubmission@health.gov.au for more information.

List of countries and jurisdictions determined to be comparable overseas regulators (CORs)

These are the countries and jurisdictions from whom the TGA will accept reports for use in the prescription medicines COR report-based process. This initial list has been determined by the Secretary for the purposes of subregulation 16DA(3) of the Therapeutic Goods Regulations 1990.

Country or Jurisdiction	Regulatory Authority
Countries	
Canada	Health Canada
Japan	Pharmaceuticals and Medical Devices Agency (PMDA)
Singapore	Health Science Authority Singapore (HSA)
Switzerland	SwissMedic
United Kingdom	Medicines and Healthcare products Regulatory Agency (MHRA)
United States	Food and Drug Administration (FDA)
Jurisdictions	
European Union	European Medicines Agency (EMA) - centralised and decentralised processes

The application of the Stage 1 criteria to the above list was significantly informed by our existing involvement in several international initiatives aimed at reducing the duplication of work across agencies and convergence of medicines regulation through information-sharing and confidence-building.

Related information

- Submission requirements
- Timeframes and milestones
- Requirements for indications

Submission requirements

COR report-based process

The information below provides guidance on the submission requirements for the prescription medicines COR report-based process.

Read this information in conjunction with other guidance on the standard prescription medicines registration process, including CTD Module 1 requirements and Mandatory requirements for an effective application.

Pre-submission planning form (PPF)

COR report-based applications must use the PPF-only pre-submission phase option available for the standard prescription medicine registration process. This means that:

- the submission must be in electronic Common Technical Document (eCTD) format
- there will be no formal Milestone 1

Applicants should proceed to lodge their entire submission for registration as soon as the complete submission number is visible on TBS. This will occur once the TGA has added the relevant stream number to the Submission ID based on the proposed indication (i.e. 'PM-yyyy-xxxxx-z-stream number').

Lodgement of a COR-A or COR-B application

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

- in Module 1.2.1 (along with the standard prescription medicines application form), the completed COR application checklist. This checklist is mandatory for COR report-based applications and helps the applicant and the TGA identify whether the application meets requirements for a COR-A or COR-B approach
  - for generic medicines: evidence that the reference product used in any assessment of bioequivalence is identical to the Australian reference product (see Guidance 15: Biopharmaceutic studies)
  - for biosimilars: also include evidence that the overseas reference product and the Australian reference product are identical (see the Regulation of biosimilars)
- in Module 1.11.1, full details of whether the application has been approved, deferred, withdrawn, rejected, approved on appeal, delayed or received a 'refusal to approve' in another jurisdiction.
  Note: This requirement seeks to capture complicated or contentious applications that require a deeper consideration of the data in the Australian context. This includes applications that have been 'indefinitely' delayed, but not situations where the application has undergone a standard 'questions' process (e.g. Day 120 List of Questions).
- in Module 1.11.4, the complete and un-redacted set of final COR assessment reports, in English

COR assessment documents

The table below lists the documents that comprise a complete assessment for each COR. The full set of documents must be submitted in your COR report-based application.

COR	Documentation
European Medicines Agency (EMA)	• Comprehensive details of all studies submitted and assessed • Centralised procedure assessment reports (where applicable): – Day 80 Quality, Non-Clinical, Clinical, and Overview Assessment Reports – Day 120 List of Questions (and answers) – Day 150 Quality, Non-Clinical, Clinical, and Overview Assessment Reports – Day 180 Joint Assessment Report – Day 180 List of Outstanding Issues – Final Assessment Report • Decentralised procedure assessment reports (where applicable): – All assessment reports – Questions from the regulator to the Market Authorisation Holder (and responses) • Summaries of meetings with the EMA and/or assessors (including presubmission advice, where relevant) • Committee for Medicinal Products for Human Use (CHMP) Summary of Opinion • Any other questions from the regulator to the Market Authorisation Holder • Letter of undertaking • European Commission decision • Risk Management Plan review(s) • Post marketing review(s) (e.g. Periodic Safety Update Reports)

COR	Documentation
Pharmaceutical and Medical Devices Agency (PMDA), Japan	• Comprehensive details of all studies submitted and assessed • Discussion documents, questions from PMDA and answers provided, and Finalised Minutes from Scientific Consultation Meetings (if applicable) • Outcome of Orphan designation, priority or SAKIGAKE determination (if relevant) • Copies of questions and answers exchanged between Sponsor and PMDA • Un-redacted English Translated Review Report consisting of: – Review Report 1 – Review Report 2 – Review Result • Report on the Deliberation Results • Approval Letter • Post-marketing review(s) (e.g. Re-examination Review Report, Periodic Safety Reports)
Health Canada	• Comprehensive details of all studies submitted and assessed • Screening: Screening Report • Clinical Review: Pharmaceutical Safety and Efficacy Assessment Report (PSEAR) • Quality: Quality Evaluation Summary (QES) and Manager's Memo • Bioequivalence: Comprehensive Summary – Bioequivalence (CS-BE) and Manager's Memo • Biostatistics: Biostatistics Consult Report (if applicable) • Risk Management Plan: Risk Management Plan Assessment Report (if applicable) • Questions from the regulator to the Market Authorisation Holder (and responses) • Summaries of meetings with Health Canada (including presubmission advice, where relevant) • Final Manager's Memo, and Executive Summary

COR	Documentation
Health Sciences Authority (HSA) Singapore	• Comprehensive details of all studies submitted and assessed • Initial Quality and Clinical reports • Questions from the regulator to the Market Authorisation Holder (and answers) • HSA assessment of responses to questions • Final Quality and Clinical summaries • Summaries of meetings with HSA (including presubmission advice, where relevant) • Approval letter • Post marketing reviews
Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom	• Comprehensive details of all studies submitted and assessed • All assessment reports as part of the iterative process • Questions from the regulator to the Market Authorisation Holder (and responses) • Committee for Medicinal Products for Human Use (CHMP) Summary of Opinion • Summaries of other meetings with the MHRA (including presubmission advice, where relevant) • Approval letter • Post marketing review(s) (e.g. Periodic Safety Update Reports)
SwissMedic, Switzerland	• Comprehensive details of all studies submitted and assessed • All assessment report(s) • Questions from the regulator to the Market Authorisation Holder (and answers) • Summaries of meetings with SwissMedic (including presubmission advice, where relevant) • Approval letter • Post marketing reviews

COR	Documentation
United States Food and Drug Administration (US FDA)	• Comprehensive details of all studies submitted and assessed • Medical review(s) • Chemistry review(s) • Pharmacology review(s) • Statistical review(s) • Clinical pharmacology biopharmaceutics review(s) • Risk assessment and risk mitigation review(s) • Administrative document(s) and correspondence • Cross discipline team leader review • Office Director memo • Summaries of meetings with the US FDA (including presubmission advice, where relevant) • Summary review • Complete response letter • Approval letter • Post marketing reviews

Where a Drug Master File (DMF) is required

Under the COR report-based process, the applicant must identify whether the application relies on a DMF.

The reports on the restricted part of the dossier (including questions raised by, and the answers provided to, the COR) must be provided to the TGA by the DMF holder along with the DMF.

How current is the information within the overseas report

The currency of information within the overseas report is a key consideration for the COR report-based process.

For COR-A applications the medicine must have received the full overseas marketing approval no longer than 1 year before the application to the TGA. This helps to ensure that TGA decisions are based on the most current international scientific and clinical information and guidelines. This also limits the likelihood that the medicine has changed since the original approval (i.e. subsequent variations).

For COR-B applications, there is no time limit for how long ago the medicine had received overseas approval. Therefore, it is more likely that the medicine or the guidelines used by the COR to assess the medicine or both may have changed.

Literature-based submissions are likely to be unsuitable for COR-A or COR-B as literature may not be current.

These factors help determine how much additional TGA evaluation effort will be required and whether a Category 1 process may be more appropriate.

Related information

- List of CORs
- Timeframes and milestones
- Requirements for indications

Timeframes and milestones

COR report-based process

The COR report-based process is associated with a shortened evaluation and decision timeframe. The aim of this process is to reduce duplication of evaluation of prescription medicines that have already been approved by a COR, while maintaining existing quality, safety and efficacy standards for medicines supplied in Australia.

The intention is that the TGA will only need to evaluate data generated specifically for the Australian context. For example, Australian labels, product information and consumer medicine information. However, in some instances, additional data may need to be considered. For example, safety data generated since the COR approval.

Consequently, we have implemented two approaches for using overseas reports:

- COR approach A (COR-A)
- COR approach B (COR-B)

The approach used will depend on the extent to which the COR report removes the need for the TGA to evaluate data. The applicant must complete and submit the COR application checklist to identify the extent of additional data which will require evaluation by the TGA. Completion of the checklist will indicate whether the application is eligible for either COR-A or COR-B.

COR approach A (COR-A)

Under COR-A, the TGA regulatory decision will be based on a critical review of the COR assessment reports and an evaluation of the Australian label, Product Information (PI) and where required, the Risk Management Plan (RMP). The evaluation and decision timeframe for COR-A applications is 120 working days.

To meet this significantly shortened timeframe, the application must meet specific requirements. Key considerations for COR-A include:

- identical medicine and manufacturing to that approved by the COR, with evidence of compliance with Good Manufacturing Practice (GMP)
- the full overseas marketing approval for the medicine is no older than 1 year
- aside from the label, PI and RMP (where required), no additional evaluation of Australian specific data is required.

COR approach B (COR-B)

Under the COR-B approach, the TGA regulatory decision will still be mostly based on a critical review of the COR assessment reports. The COR-B process has a 175 working day evaluation and decision timeframe, allowing for TGA evaluation of certain data, in addition to the label, PI and RMP.

The amount and type of additional data requiring evaluation will determine whether the application is best processed under the COR-B approach or as a Category 1 application.

Examples of additional data that may be considered under the COR-B process include updated stability data, validation data for an additional manufacturing site and updates to pivotal studies that support the proposed indication.

Related information

- List of CORs
- Submission requirements
- Requirements for indications
- Prescription medicines application forms

Requirements for indications

COR report-based process

Criterion 5 of the COR criteria states that indications for the medicine proposed for supply in Australia must be equivalent to that approved by the COR.

Criterion 5 also states that broadly similar population demographics, disease profiles, and expectations regarding public health outcomes should apply to both Australia and the overseas jurisdiction.

We understand that between countries:

- indications may differ in the way they are reflected in the local clinical practice, even where they are based on the same clinical data set
- indications may differ because of different clinical needs in different geographic areas
- for generics and biosimilars, the indications will be dictated by the indication of the originator product in each respective country. There is no guarantee that these are currently aligned across countries.

For COR report-based applications indications must be equivalent, but not necessarily identical. Acceptable differences between the approved and proposed indication 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 and outcome

For generics and biosimilars, the proposed indication must be identical to the indication approved for the originator within Australia.

Related information

TGA has adopted the EMA guideline on Ethnic Factors in the Acceptability of Foreign Clinical Data (CPMP/ICH/289/95 ICH Topic E 5 (R1) Note for Guidance on Ethnic Factors in the Acceptability of Foreign Clinical Data).

Related information

- List of CORs
- Submission requirements
- Timeframes and milestones

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Scientific Evaluation Branch	January 2018
V1.1	Minor clarifications to the COR report-based process requirements and updated links to related information. Publication of the list of CORs taking part in work-sharing with the TGA.	Scientific Evaluation Branch	June 2018
V1.2	Addition of Japan to the list of CORs Removal of references to work-share Additional clarity for some criteria	Prescription Medicines Authorisation Branch	October 2019

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