



Australian Government
Department of Health
Therapeutic Goods Administration

Prescription medicines registration process

Version 2.5, August 2021

TGA Health Safety
Regulation



Copyright

© Commonwealth of Australia 2021

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

1. Introduction	6
2. Overview	7
2.1 Scope	7
2.2 Regulatory and supporting documents	7
2.3 Terminology	8
Application	8
Application category	8
Application type	8
Dossier	8
Submission	9
2.4 Key regulatory requirements	9
2.4.1 Management by milestones	9
2.4.2 Quality of applications	9
2.4.3 Pre-submission phase	9
2.4.4 Submission phase	10
2.4.5 Priority review designated applications	10
2.4.6. Provisional approval pathway	10
2.5 Information	11
2.5.1 Solicited information	11
2.5.2 Unsolicited information	12
2.5.3 Safety data	12
3. Planning and tracking of applications	14
3.1 Regulatory phases	14
3.2 Regulatory timelines	15
3.3 Submission planning	15
3.4 Submission tracking	16
4. Pre-process activities	17
4.1 Pre-submission meetings	17
4.2 Availability of dossier	17
4.3 Pre-conditions	17
4.3.1 Orphan drug applications	17
4.3.2 Literature-based submissions	18
4.3.3 Fixed combination applications	18

4.3.4 Ingredients	18
4.3.5 Genetically modified organisms (GMOs)	19
4.3.6 Medicines scheduling	19
4.3.7 Concurrent applications	19
5. Registration process phases _____	22
5.1 Phase 1: Pre-submission phase _____	22
5.1.1 Objective	22
5.1.2 Milestone 1	22
5.1.3 Key dates	22
5.1.4 Requirements at pre-submission	22
5.1.5 Lodging a pre-submission planning form	23
5.1.6 Change of details after pre-submission	24
5.1.7 Application dates	24
5.1.8 What happens if an applicant misses a key date?	24
5.2 Phase 2: Submission phase _____	25
5.2.1 Objective	25
5.2.2 Milestone 2	25
5.2.3 Key dates	25
5.2.4 Lodgement of application	26
5.2.5 Processing the application	26
5.2.6 What happens if an applicant misses a key date?	27
5.3 Phase 3: First round assessment phase _____	28
5.3.1 Objective	28
5.3.2 Milestone 3	28
5.3.3 Key dates	28
5.3.4 Assessment of data	28
5.3.5 First round assessment reports	28
5.4 Phase 4: Consolidated section 31 request response phase _____	29
5.4.1 Objective	29
5.4.2 Milestone 4	29
5.4.3 Key dates	29
5.4.4 Response to section 31 request	29
5.4.5 Response to first round assessment reports	29
5.4.6 What happens if an applicant misses a key date?	30
5.5 Phase 5: Second round assessment phase _____	31
5.5.1 Objective	31
5.5.2 Milestone 5	31

5.5.3 Key dates-----	31
5.5.4 Assessment of response -----	31
5.5.5 Opportunity to review evaluation reports -----	31
5.6 Phase 6: Expert advisory review phase _____	32
5.6.1 Objective -----	32
5.6.2 Milestone 6 -----	32
5.6.3 Key dates-----	32
5.6.4 Advisory Committee on Medicines -----	32
5.6.5 Pharmaceutical subcommittee -----	Error! Bookmark not defined.
5.6.6 What happens if an applicant misses a key date?-----	36
5.7 Phase 7: Decision phase _____	37
5.7.1 Objective -----	37
5.7.2 Milestone 7 -----	37
5.7.3 Key dates-----	37
5.7.4 Review and decision -----	38
5.7.5 What happens if an applicant misses a key date?-----	39
5.8 Phase 8: Post-decision phase _____	40
5.8.1 Objective -----	40
5.8.2 Milestone 8 -----	40
5.8.3 Key dates-----	40
5.8.4 ARTG registration -----	40
5.8.5 Medicines information -----	40
5.8.6 What happens if an applicant misses a key date?-----	41
Appendix 1 - Sample timelines _____	42
Appendix 2 - Registration process regulatory phases	45

1. Introduction

The TGA registration process for prescription medicine applications, that need to be supported by nonclinical, clinical and/or bioequivalence data (category 1 and category 2). This regulatory process is designed to improve the efficiency and timeliness of the registration of prescription medicines without compromising the scientific rigour of the evaluation process, thus ensuring the maintenance of appropriate standards of quality, safety, and efficacy. This document describes this process and outlines the relevant regulatory requirements.

The key elements of this process are:

- management by milestones
- an improved quality of dossiers prepared in accordance with common technical document (CTD) format and other TGA regulatory requirements
- a pre-submission planning phase where applicants lodge details of a proposed application at least 2¼ months prior to lodgement of the dossier allowing the TGA to identify milestone dates and plan resource requirements (this is not required for submissions lodged in eCTD format if the sponsor selects the PPF-only option)
- submission phase where the applicant must lodge a complete dossier, there being no opportunity to deliver new data after the submission date except as required by the [Therapeutic Goods Act 1989](#) (the Act)
- requests for information under section 31 of the Act are consolidated and issued at the end of the initial evaluation phase.

[Legislative instruments](#) made under section 9D and section 23 of the Act support this process. These instruments provide the legislative basis for the documents that specify the regulatory requirements for applications lodged under this process.

2. Overview

2.1 Scope

This document provides an overview of the TGA's registration process for applications that need to be supported by nonclinical, clinical and/or bioequivalence data (category 1 and category 2).

Applications to vary a product registration (section 9D of [the Act](#)) and not supported by nonclinical, clinical and/or bioequivalence data are outside the scope of this document.

2.2 Regulatory and supporting documents

Category 1 and 2 applications for new registrations are made under section 23 of the Act. Section 23 requires that applications are made in a form approved by the Secretary. The currently approved form is the CTD format.

Category 1 and 2 requests to vary the entry in the Australian Register of Therapeutic Goods (ARTG) of registered therapeutic goods are made under section 9D of the Act. Section 9D requires that applications are made in a manner approved by the Secretary. The currently approved manner is the CTD format.

The CTD format is described in the following documents:

- [CTD Module 1: Administrative information and prescribing information for Australia](#)
- [ICH M4Q Common technical document for the registration of pharmaceuticals for human use-Quality \(CPMP/ICH/2887/99 Rev 1 Quality\)](#)
- [ICH M4S Common technical document for the registration of pharmaceuticals for human use-Safety \(CPMP/ICH/2997/99 Rev 1 Safety\)](#)
- [ICH M4E Common technical document for the registration of pharmaceuticals for human use-Efficacy \(CPMP/ICH/2887/99 Rev 1 Efficacy\)](#).

For category 1 and 2 applications, other than applications solely for an additional trade name, the [section 23 and section 9D instruments](#) specify applications must comply with the following regulatory documents:

- [Mandatory requirements for an effective application](#)
- [Pre-submission planning form](#)
- prescription medicines (PREMIER) electronic lodgement facility (for applications to register a new chemical entity, new fixed combination, similar biological medicinal product or a new generic medicine)

or

- the form [Application for the registration, or to vary the conditions of registration, of prescription medicines](#) (all other applications)

In addition to the documents specified by the section 9D and section 23 instruments, the TGA has produced other documents which provide further assistance for applicants who are lodging a PPF or dossier. These include:

- [Prescription medicine registration process](#) (this document)
- [Information for applicants completing a pre-submission planning form](#)
- [Electronic format requirements for industry for providing regulatory information: Non eCTD electronic submissions \(NeeS\) for human medicinal products](#)

2.3 Terminology

Application

- Application refers to the regulatory activity required in respect of a product (a specific set of formulations, strengths and presentations) as requested by the applicant of the product.
- It is the specific set of information on the product submitted for review.
- Examples include:
 - an application for the registration of a new medicine
 - registration of a new indication.

Application category

- Application category is identified by a number, for example, category 1 and category 2 applications, and refers to the overall legislated time-frames for decisions about applications.

Application type

- Application type relates to the fees associated with an application and is identified by a letter, for example, A, B or C application types.
- Examples include:
 - new chemical entity
 - new indication or major variation.

Dossier

- A dossier contains and/or references the necessary data to demonstrate the quality, safety and efficacy of a prescription medicine.
- The supporting data consists of:
 - the dossier lodged in the first instance
 - any dossiers provided to the TGA previously that are referenced by the application
 - any other data to support the application that is lodged following initial lodgement of the application (for example, section 31 responses, further safety data).

Submission

A submission is a collection of one or more applications that are grouped together for fee purposes, and is specific to a particular active ingredient and applicant.



It is the applicant's responsibility to identify all application types that are included in a submission by selecting all applicable types in Part C of the [application form](#). Only those application types that are identified in the form will be evaluated for registration in the Australian Register of Therapeutic Goods (ARTG). For example, if you are seeking an extension of indication and an additional change to the product information, a type C application under S23 and a separate type J application under 9D must be indicated in order for the applications to exist individually. The highest fee category applies where multiple application types are included in a submission.

2.4 Key regulatory requirements

2.4.1 Management by milestones

The registration process consists of eight phases with eight milestones, allowing effective planning and tracking by the TGA and applicants. Each phase has established timeframes.

To facilitate management by milestones, all applications received in a given intake will proceed as a group through the phases and milestones, a process known as 'batch processing'.

2.4.2 Quality of applications

For the TGA to ensure that planned and target timeframes are met, it is critical that applicants lodge well-planned, high quality applications. Should a dossier not meet the regulatory requirements, it will be considered 'not effective' and will not be accepted for evaluation.

It is not possible for applicants who submit incomplete, delayed, or poor quality applications to provide unsolicited information during the regulatory process to rectify these deficiencies.

2.4.3 Pre-submission phase

Under the registration process, applicants provide the TGA with planning data in the *Pre-submission planning form* (PPF) at the pre-submission phase. Planning data include general submission information as well as information about the proposed application type and details of the quality, nonclinical and clinical evidence that will be provided in the dossier. The PPF provides the TGA with the necessary information for effective resource planning.

If the TGA considers a PPF complete and acceptable, the applicant will receive a *Planning letter* that provides key dates for the phases and milestones of the regulatory process for the application.



Comment

Pre-submission meetings may be requested where appropriate—the pre-submission phase does not replace the opportunity for applicants to conduct face-to-face discussions with the TGA regarding aspects of their proposed application. Pre-submission meetings may occur at any stage prior to PPF lodgement.

Meetings between TGA and applicants are conducted according to the processes described in the guideline [Pre-submission meetings with the TGA](#). The TGA point of contact should be the PSAB Case Manager of the relevant clinical evaluation unit. Information on the areas of responsibility for the clinical units is included in [Clinical evaluation sections for prescription medicines](#).

2.4.4 Submission phase

Applicants provide a dossier for evaluation at the submission phase. Applicants must ensure applications meet TGA regulatory requirements for format and content or the application will be considered ‘not effective’ and will not be accepted for evaluation. There will be no requests for information or documents under section 31 of the Act at the submission phase to address deficiencies in applications that do not meet TGA requirements.

Applications must be received by the date noted in the *Planning letter* to allow the TGA to complete the necessary administrative activities by the end of the same month.

At the end of the submission phase, the TGA will send the applicant a *Notification letter* advising that the application has either:

- been considered effective and is accepted for evaluation
- or
- been considered ‘not effective’ and is not accepted for evaluation.

2.4.5 Priority review designated applications

TGA now has a formal Priority review pathway for faster assessment of vital and life-saving prescription medicines for which a complete data dossier is available. The target timeframe of 150 working days is up to three months shorter than the standard prescription medicines registration process. A valid [Priority review designation](#) must be held in order to access the Priority review pathway. More information on Priority review is available at:

- [Priority review designation: A step-by-step guide for prescription medicines](#)
- [Priority review designation eligibility criteria: Including supporting documentation](#)
- [Priority review registration process](#)

2.4.6. Provisional approval pathway

The TGA now has a formal [Provisional approval pathway](#) for the provisional registration of prescription medicines on the basis of preliminary clinical data, where there is the potential for a substantial benefit to Australian patients. A valid Provisional determination must be held in order to access this pathway.

More information on Provisional approval is available at:

- [Provisional approval determination: A step-by-step guide for prescription medicine](#)
- [Provisional approval determination eligibility criteria: Including supporting documentation](#)
- [Provisional registration process: a step-by step guide for prescription medicines](#)
- [Provisional registration extension and transition to full registration](#)

2.5 Information

Applications must contain all the information and material required for purposes of section 9D or section 23 of the Act and the documentation presented at submission will be taken as the complete application.

The applicant certifies in the PPF that the content of the complete dossier aligns with the information provided in the PPF and that the dossier, as received by the TGA, will be considered to be the full and complete dossier notwithstanding any further data requested by the TGA (including under section 31 of the Act) and/or new safety related data, which the applicant is obliged to bring to the TGA's attention. Applicants are strongly advised not to lodge a PPF before the full extent of the supporting data necessary for the application to be evaluated is known to be available.

To assist applicants prepare a complete application, TGA has published numerous documents and guidelines on the preparation and submission of prescription medicine applications. Applicants of prescription medicine applications should refer regularly to the TGA web site for those guidelines and policies relating to a particular application type of interest. Where a relevant guideline is not met, an appropriate justification must be provided in the dossier.

Once an applicant has submitted the dossier to TGA any data received by TGA without being requested by TGA will be considered 'unsolicited information'.

Data submitted after submission of the dossier must be accompanied by a covering letter which includes the submission number of the relevant application, the purpose of the correspondence and whether the information and material is 'solicited' or 'unsolicited'.

2.5.1 Solicited information

TGA considers the following to be solicited information:

- information and documents sent in response to the consolidated section 31 request following the first round assessment phase. The request will be sent on the date identified in the Notification letter allowing applicants time to conduct any necessary preparation activities.
- responses to informal requests from TGA staff for information or documents (for minor issues and clarifications). These requests may occur throughout the evaluation process and are intended only to maintain efficiency in the evaluation process, not to rectify deficiencies in incomplete or poor quality applications.

All solicited information in response to questions should be submitted in a question and answer format which is cross-referenced to replacement volumes where appropriate.

Applicants will also be able to:

- comment on the evaluation reports to highlight any errors of fact or major omissions

- comment (pre-ACM/ACV response) on the delegate's request for advice from the independent Advisory Committee on Medicines (ACM) or Advisory Committee on Vaccines (ACV) when such advice is sought.

2.5.2 Unsolicited information

TGA will accept the following unsolicited information for evaluation:

- safety data (see 2.5.3 for the definition of safety data). Applicants are obligated to inform the TGA as soon as new safety data becomes available.
- new/renewed/updated TGA manufacturing licences (for Australian manufacturing sites) and good manufacturing practice (GMP) clearances (for overseas sites) issued for those sites identified in the application.
- revised trade names. An applicant may change, but not add, a trade name at any time prior to the end of the second round assessment phase.

In the event that the TGA receives other unsolicited information from an applicant, the applicant should be aware that there is a likelihood that the TGA **will not evaluate the data**. Applicants must, therefore, ensure that their dossier contains the full data set that they wish the TGA to evaluate and that the mandatory requirements (as applicable to the nature of the medicine and application type) are met.

The TGA will work with applicants of medicines of critical importance to the Australian community in emergency situations to ensure this policy does not adversely affect the timely evaluation of such medicines. Applicants of such medicines are encouraged to discuss arrangements with the TGA at a pre-submission meeting and in any case, as early as possible.

2.5.3 Safety data

For the purposes of the registration process, new safety data refers to information that might negatively influence the benefit-risk assessment of a medicinal product. Examples include but are not limited to:

- a. an increase in the rate of occurrence of an "expected," serious adverse drug reaction which is judged to be clinically important
- b. a significant hazard to the patient population, such as emergent lack of efficacy with a medicinal product used in treating a life-threatening disease, or a spate of unlisted reports of an uncommon or rare but serious adverse event
- c. a major safety finding from a newly completed animal study (such as an increased incidence of tumours in treated animals)
- d. pooled analyses of clinical studies that suggest significant dose or time dependent adverse effects that were neither apparent nor available at the time of lodging the application
- e. safety data associated with regulatory action in the event of, or to prevent risk to public health associated with use of the product in countries where it is already registered.

Safety data in this context do not include, for example:









- a. studies which only confirm information previously submitted to the TGA, including extension studies of submitted nonclinical or clinical studies (i.e. a, b and c above do not apply)

- b. studies or other data which support the use of the medicine in accordance with the proposed recommendations but which do not identify a new unexpected adverse drug event or an increased incidence of an expected adverse drug event
- c. pharmaceutical data
- d. nonclinical studies to justify proposed impurity limits.

3. Planning and tracking of applications

3.1 Regulatory phases

The regulatory process for evaluation of prescription medicines consists of eight phases. Each phase has a milestone that must be completed before commencement of the following phase. This approach allows effective and transparent management of resources and timelines for all applications.

Phase	Relevant milestone	
1 - Pre-submission	 MS1	Outcome of pre-submission planning sent
2 - Submission	 MS2	Outcome of application consideration sent
3 - First round assessment	 MS3	Outcome of first round assessment and section 31 request for information or documents sent
4 - Consolidated section 31 request response	 MS4	End of section 31 request response period
5 - Second round assessment	 MS5	Outcome of second round assessments sent
6 - Expert advisory review	 MS6	Outcome of expert advisory committee review sent
7 - Decision	 MS7	Decision made by delegate
8 - Post-decision	 MS8	Administrative and regulatory activities complete

Appendix 2 contains a pictorial representation of the regulatory phases. Section 5 of this document provides details about each of the phases.

3.2 Regulatory timelines

Depending on the type of application, different phases will be required which will affect the overall timeframe for the regulatory process. For initial planning purposes, applications are categorised into four distinct groups that are covered by some or all regulatory phases.

- Default plan ○ Optional

	Pre-submission	Submission	First round assessment	Consolidated section 31 response	Second round assessment	Expert advisory review	Decision	Post-decision
New chemical entities, extensions of indications	●	●	●	●	●	●	●	●
Generic medicines	●	●	●	●	●	○	●	●
PI changes, variations to existing products	●	●	●	●	●	○	●	●
Additional trade names		●	●	○	○		●	●

The registration process introduces planning timeframes into each of the phases, as indicated in appendix 4 and section 5 of this document. While the legislated TGA commitment of 40 working days between receipt of an application and notification of acceptance or rejection of that application remains, under the registration process this phase (the submission phase) will typically be completed in 15 or 21 calendar days, unless otherwise advised in the *Planning letter*.

The legislated TGA commitment of 255 working days between acceptance for evaluation through to the delegate's decision will also remain but will not be used for planning or for target times. The registration process is designed to take, on average, 330 calendar days (11 months), including the time for applicant activities.

Examples of timelines showing target milestone timeframes is provided in Appendix 1.

3.3 Submission planning

Planning for the evaluation process occurs during the pre-submission phase where the application type, the product, the scope and scale of the application, and the date of proposed dossier lodgement are identified. The information provided in the PPF allows the TGA to identify the resources required, including the specific areas of expertise, to evaluate an application. This phase also allows for the identification of any circumstances that may require the standard timeframe to be altered. Applicants will be notified of any alterations to the target timeframes.

Under the registration process, the TGA begins allocating resources for the evaluation phase when the PPF is lodged. These resources are based on the expected date of dossier lodgement. If a dossier does not arrive by the expected date, the TGA will reallocate the resources for that

application and the applicant must re-commence the regulatory process from the beginning by lodging another PPF.

3.4 Submission tracking

Once the PPF is lodged, the TGA will track the application through the regulatory process. Each phase of the regulatory process concludes with the completion of a milestone.

At key points in the registration process TGA will notify the applicant of the evaluation plan milestone dates: an evaluation plan is included in the Planning letter at Milestone 1, the Notification letter at Milestone 2 and the Milestone 3 letter at Milestone 3. As target timeframes may change, applicants should always consult the most recent letter.

To facilitate tracking, the TGA has implemented a single email address streamlinedsubmission@tga.gov.au for the applicant through which formal correspondence will be coordinated. The TGA point of contact should be the PSAB Case Manager of the relevant clinical evaluation unit. Information on the areas of responsibility for the clinical units is included in [Clinical evaluation sections for prescription medicines](#).

4. Pre-process activities

4.1 Pre-submission meetings

Applicants may wish to discuss scientific or procedural issues with the TGA in a pre-submission meeting prior to preparing a PPF or dossier. Such discussions should occur well in advance of PPF and dossier lodgement. The TGA strongly recommends that applicants organise a pre-submission meeting for complex applications. Meetings between TGA and applicants are conducted according to the processes described in the guideline [Pre-submission meetings with the TGA](#). Applicants will need to provide details in the PPF and the dossier (Module 1.8.1) of any meetings conducted with the TGA.

4.2 Availability of dossier

The PPF requires applicants to identify a proposed dossier lodgement date. Applicants should not lodge a PPF until they are confident all the data necessary for the evaluation of the application will be ready for delivery on the proposed dossier lodgement date.

A dossier that was lodged previously with the TGA but not accepted for evaluation may be re-used in certain circumstances:

Reason	Dossier can be reused?	Comments
Not accepted solely because dossier not lodged by required date	Yes - partially	The majority of the paper dossier can be re-used provided Modules 2 to 5 do not need to be updated or otherwise modified with new information. A revised paper copy of Module 1 must be provided. A complete electronic version of the revised dossier must be lodged.
Any other reason	No	The complete dossier must be re-lodged. The applicant retains responsibility for providing the TGA with the appropriate dossier to be evaluated.

4.3 Pre-conditions

Applicants may need to fulfil a number of pre-conditions before lodging a PPF. In some cases, evidence is required in the PPF that the approval process has commenced on related activities. These are described below.

4.3.1 Orphan drug applications

For designated orphan drugs, the Secretary waives application and evaluation fees for the evaluation of a medicine for the purposes of registration. For fees to be waived, the applicant must apply for, and be granted by the TGA, orphan drug designation before lodging the PPF. Further information about making such a request can be found in:

- [Applications for orphan drug designation](#).

Discussions with the TGA regarding orphan drug applications should commence well before the pre-submission phase. Applications for orphan drug designation should be lodged with the TGA

two to three months before the intended start of the pre-submission phase. If an applicant has not received approval for the designation but chooses to proceed with the application, they become liable for the relevant application and evaluation fees.

4.3.2 Literature-based submissions

For applications using literature references as all or part of the supporting data set, the applicant must seek the TGA's agreement on the following before lodging the PPF:

- the search strategy employed
- the databases to be searched
- the criteria for determining which papers identified by the search results are to be included/excluded from the dossier.

These requirements are necessary because the data provided in the dossier is dependent on the search strategy. Applicants should plan to discuss these issues with the TGA at least three months prior to the pre-submission phase. Further information on literature-based submissions is provided in [Literature-based submissions](#).

4.3.3 Fixed combination applications

For a new fixed combination product the applicant must justify, prior to lodging a PPF, the particular combination and the type and extent of data to be provided in the dossier. This is done by preparing and lodging with the TGA a 'justification for fixed combination'. This is a letter to the TGA that presents the case for the fixed combination, prepared according to the following EU guidelines that have been adopted in Australia:

- [CHMP/EWP/240/95 Rev. 1 - Guideline on clinical development of fixed combination medicinal products](#)
- [EMA/CHMP/SWP/258498/2005 - Guideline on the non-clinical development of fixed combinations of medicinal products](#).

If one or more of the component active ingredients of the fixed combination product is/are not registered, the justification must include the proposed dossier lodgement dates for the unregistered components and the fixed combination product.

4.3.4 Ingredients

The TGA maintains databases of proprietary and non-proprietary ingredients which can be accessed from the TGA's [eBS portal](#). Where an applicant wishes to register a new product that contains a new ingredient (one that is not on the databases), the applicant must commence, before lodging the PPF, the process for approval of a new ingredient for inclusion on the relevant databases.

For each new ingredient, the following forms must be lodged:

- a [Notification of a New Proprietary Ingredient](#) for each new proprietary ingredient
- an [application form for proposing a new chemical name](#) (AAN), biological name (ABN) and/or herbal name (AHN) for each new non-proprietary ingredient.

Refer to part 2.1 of [Information for applicants completing a pre-submission planning form](#) for details on accessing the ingredient databases and the location of forms.

**Note**

Unless justified, toxicology data must be provided to the TGA to support the safety of an existing ingredient that is to be used for different purposes to that originally approved, for example, a new route of administration.

4.3.5 Genetically modified organisms (GMOs)

It is likely that approval from the Office of the Gene Technology Regulator (OGTR) is required for medicines that:

- contain GMO(s)
- consist of GMO(s)
- are manufactured in Australia and are derived from GMOs.

In such circumstances, applicants must apply to the [OGTR](#) for a licence, an exemption, or a Notifiable Low Risk Dealing approval, before lodging the PPF. Any OGTR advice (for example, OGTR licence, acknowledgement of receipt of licence application, other record of consent) must be provided to the TGA with the PPF.

4.3.6 Medicines scheduling

Where a proposed application relies upon the rescheduling of an existing substance in the [Poisons Standard](#), applicants must lodge an application for rescheduling prior to lodging the PPF:

- [Application to Amend the Poisons Standard](#)

4.3.7 Concurrent applications

Applications to amend any details for a product cannot be lodged until the product is listed on the ARTG. If an applicant wishes to make changes to a proposed product, the application cannot be lodged until the registration process is finalised. The same requirement applies to a new chemical entity application currently under evaluation and a proposed new combination application (where the product contains the new chemical entity under evaluation).

Where a product is already registered and there is an existing application (variation or registration) currently with the TGA, it is acceptable to lodge a concurrent application in certain circumstances, provided that the changes proposed in the applications are unrelated. The following table indicates when it may be appropriate to lodge concurrent applications.

		Application currently with the TGA		
		Resulting in new Register entry ¹ with new AUST R	Resulting in new Register entry ¹ but no new AUST R	Not resulting in a new Register entry ¹
Proposed application	Resulting in new Register entry ¹ with new AUST R	<p>Proposed application can be lodged only if new products covered in the proposed application are based on an existing Register entry.</p> <p>If not, proposed application should be postponed until application under evaluation has been approved and the ARTG updated.</p>	<p>Proposed application can be lodged only if the changes currently under evaluation are not to apply to the new products covered in the proposed application.</p>	<p>Proposed application should be postponed until application under evaluation has been approved and the ARTG updated.</p>
	Resulting in new Register entry but no new AUST R	<p>Proposed application can be lodged only if changes are to apply to existing Register entries only.</p> <p>If not, proposed application should be postponed until application under evaluation has been approved and the ARTG updated.</p>	<p>Can be lodged, provided the changes in the current and proposed applications are unrelated.</p>	<p>Can be lodged, provided the changes in the current and proposed applications are unrelated.</p>
	Not resulting in a new Register entry	<p>Proposed application can be lodged only if changes are to apply to existing Register entries only.</p> <p>If not, proposed application should be postponed until application under evaluation has been approved and the ARTG updated.</p>	<p>Can be lodged, provided the changes in the current and proposed applications are unrelated.</p>	<p>Can be lodged, provided the changes in the current and proposed applications are unrelated.</p>

¹ A new registration (or new Register entry) is one that requires a new ARTG entry by reason of being 'separate and distinct goods' under s.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, extensions of indication. However, not all new registrations will result in a new AUST R number being allocated if they are taken to be grouped by reason of the Therapeutic Goods (Groups) Order 2001.

If unsure of regulatory requirements where a related application is under consideration, applicants should contact the TGA before lodging a PPF for an application. Where there is a potential relationship between an application currently under evaluation and the proposed application, this must be indicated in the PPF.

Where the proposed application seeks changes to an entry in the Register under section 9D of [the Act](#) and would result in changes to the product information document currently under evaluation, such changes to the document currently under evaluation must be identified, either in the product information document or the letter of application of the proposed application.

**Note**

In cases where a concurrent application is acceptable and an applicant chooses to lodge a concurrent application, the applicant assumes a level of risk. This is particularly so in cases where the outcome of the initial application is unknown. It is possible that an application may be considered not effective if, for example:

- the outcome of the initial application is negative
- the evaluation on the initial application has not progressed sufficiently.

5. Registration process phases

5.1 Phase 1: Pre-submission phase

5.1.1 Objective

The pre-submission phase applies to category 1 and category 2 applications, excluding requests for additional trade names.

The pre-submission phase begins with the lodgement of the *Pre-submission planning form* (PPF). The PPF provides the TGA with the necessary information on the scope and scale of an application to arrange appropriate resourcing for the processing and evaluation of the application. Once a PPF has been considered complete and acceptable, the TGA begins the process of securing appropriate evaluators for the dossier.

A complete PPF identifies the proposed application type, and contains general information about the quality, nonclinical, and clinical evidence to be included in the dossier. The information provided in the PPF allows the TGA to commit to timeframes for the evaluation of the application.

5.1.2 Milestone 1

If the PPF is considered complete and acceptable, a TGA Planning letter is sent to the applicant identifying the expected dossier lodgement date and target milestone dates for the application.

5.1.3 Key dates

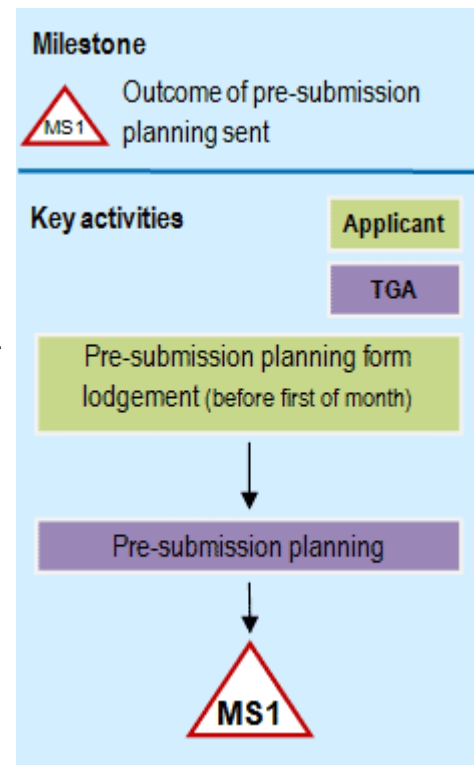
The pre-submission phase commences with the lodgement of a PPF. PPFs are processed on the first day of each month.

The submission phase concludes when TGA sends the applicant a Planning letter. This letter is sent to applicants before or on the fifteenth of the month following the month in which the PPF was initially processed (or the following working day where the fifteenth of the month falls on a weekend or [public holiday](#) in the Australian Capital Territory).

5.1.4 Requirements at pre-submission

5.1.4.1 Pre-submission planning form

Applicants must complete and lodge a [Pre-submission planning form](#). All sections of the PPF that are relevant to the proposed application must be completed. [Information for applicants completing a pre-submission planning form](#) is a step-by-step guide for applicants completing a PPF. If the applicant does not complete all relevant sections and provide the necessary documents as attachments, the TGA will consider the PPF not complete and not acceptable. Should the applicant wish to proceed with the registration of the medicine or the variation to the register entry, they will need to lodge a new PPF.



5.1.4.2 Module 2 data

A key element of the PPF is the provision of Module 2 (or equivalent) data which contains information on the scope, scale, and complexity of the proposed dossier. The TGA encourages the attachment of a complete CTD Module 2. The requirements for module 2 content at the pre-submission phase are explained in more detail in the [Pre-submission planning form](#) and [Information for applicants completing a pre-submission planning form](#).

The TGA uses the information lodged by applicants in the PPF to plan the necessary resourcing to process and evaluate the application and to commit to milestone dates in the Planning letter. The information is particularly crucial when the TGA needs to secure external evaluators.

5.1.5 Lodging a pre-submission planning form

5.1.5.1 On-line form via eBS

Completion and lodgement of a PPF is a two-step process that uses the TGA's secure eBS portal (see [Information for applicants completing a pre-submission planning form](#).)



Comment

The PPF is currently downloaded from the TGA website, completed, and lodged with the TGA through eBS. The TGA is working to develop an online smart form in eBS to replace this document. Smart form technology will allow the form to be pre-populated with automatically retrieved applicant information.

5.1.5.2 Certification by applicant

The applicant must declare on the PPF that they understand the TGA's requirements for an effective application and that the application will be processed by the TGA in accordance with the procedures described in *Prescription medicine registration process* (this document).

The TGA's requirements for an effective application are established through [legislative instruments](#) made under section 9D and section 23 of the Act. Under these instruments, the planning information provided at pre-submission, along with the application form, and dossier (containing data for evaluation) comprise the information required under section 9D and section 23 of the Act to allow determination of the application.

5.1.5.3 Application fee

Upon lodgement of a PPF, applicants become liable to pay the application fee². The application fee allows the TGA to recover the costs associated with processing the PPF and arranging evaluation resources. If a PPF is considered 'not effective' or the dossier is not subsequently accepted for evaluation, the applicant will forfeit this application fee. An application cannot be considered effective if the application fee has not been paid.

The application fee amounts are available at the [fees and payments](#) section of the TGA website.

² An application fee is not payable for applications made under section 23 of the Act and involving a medicine which has been designated an orphan drug.

5.1.6 Change of details after pre-submission

The TGA *Planning letter* (issued when a PPF is considered complete and acceptable) contains:

- the lodgement date for the dossier
- the expected dates for the milestones of the regulatory process
- any issues the TGA has identified when considering the PPF which need to be addressed in the dossier. For example, the TGA may indicate whether a proposed justification is not sound, giving the applicant time to make amendments before dossier lodgement.

When lodging the PPF, the applicant declares that they will provide a complete application dossier, the contents of which align with the information provided in the PPF, by the date that they have specified in the PPF. If it appears that the scope or scale of the dossier will be different to that described in the PPF, there is a risk that the application will be considered 'not effective'. Examples of changes that are likely to result in an application being considered 'not effective' include:

- a significant change of proposed indication or addition of an indication
- an increase in the number of studies that form key sources of evidence (including, but not limited to, pivotal phase III studies, biopharmaceutical studies and carcinogenicity studies)
- a new strength
- an additional trade name.

The TGA recognises that some information may change before a dossier is lodged, for example, new [safety information](#) becomes available or further information needs to be included to address issues that the TGA raises in the *Planning letter*. Where the information that needs to be included impacts on the scope and scale of the application, applicants are advised to contact the TGA before lodging the application dossier.

Any differences between the dossier and the information provided in the PPF must be acknowledged in the covering letter for the dossier then described in detail and justified in *Module 1.8.3: Declaration of compliance with the pre-submission planning form and planning letter*. Refer to [CTD Module 1](#) for more information on preparing these documents.

Applicants should note that where the application differs in scope or scale from that described in the PPF but the TGA agrees to proceed with evaluation, the TGA will need to reassess resources and may need to adjust milestone dates accordingly.

5.1.7 Application dates

The TGA *Planning letter* outlines the key dates for each phase of the regulatory process, including the expected date of dossier lodgement. The dossier may be lodged any time between the receipt of the *Planning letter* and close of business on the expected date of lodgement identified in the *Planning letter*. Applicants are encouraged to lodge their dossier as early as possible. However, early lodgement of the dossier will not result in an earlier achievement of milestone 2.

The *Planning letter* also identifies the date on which it is proposed to send the section 31 request for information or documents to the applicant and the date by which the applicant must respond to the request. This allows applicants to prepare to address any issues raised.

5.1.8 What happens if an applicant misses a key date?

To be included in a given monthly batch, the PPF must be received on or before the day preceding the first day of each month. A PPF lodged on the first day of a month will not be processed until the following month.

5.2 Phase 2: Submission phase

5.2.1 Objective

The submission phase involves processing activities in preparation for application evaluation. For the TGA, processing activities include:

- confirmation of dossier delivery by the expected lodgement date
- verification that any application fee has been paid
- workflow planning and IT administration
- consideration of the application against the TGA regulatory requirements
- issuing of a Notification letter, including notice of evaluation fee payable, if applicable.

5.2.2 Milestone 2

The TGA sends a letter to the applicant identifying whether the application has been considered effective and accepted for evaluation, or considered 'not effective'.

5.2.3 Key dates

The submission phase commences with receipt of the dossier. The dossier is expected to contain all the information required by the TGA to evaluate the application(s).

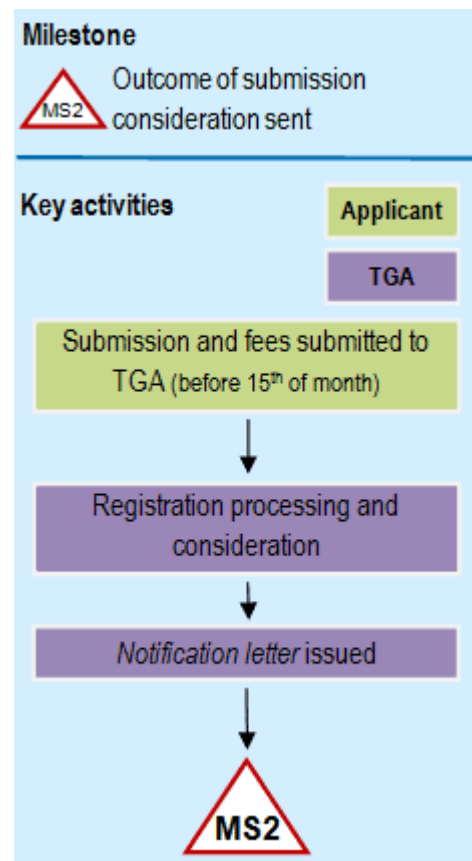
For applications to register:

- a new chemical entity
- a new biological entity
- a new fixed combination
- a similar biological medicinal product
- an extension of indications

the dossier must be received by TGA before close of business (5.00 pm) on the seventh of the month following receipt of the *Planning letter* (or the following working day where the seventh falls on a weekend or [public holiday](#) in the Australian Capital Territory), unless another date is specified in the *Planning letter*.

For applications to:

- register a major variation
- register a minor variation
- register a new generic medicine
- vary the PI



the dossier must be received by TGA before close of business (5.00 pm) on the 14th of the month following receipt of the *Planning letter* (or the following working day where the fourteenth falls on a weekend or public holiday in the Australian Capital Territory).

The submission phase concludes when TGA sends the applicant a *Notification letter*. This letter is sent to applicants before the end of the month in which the dossier was lodged (or the following working day where the last day of the month falls on a weekend or public holiday in the Australian Capital Territory).

The *Notification letter* will advise the applicant whether the application is effective or not (Section 9D(7) and Section 23 of the Act). If an application is considered not effective the *Notification letter* will explain why it was considered not effective.

5.2.4 Lodgement of application

Applicants of all new chemical entity, new fixed combination, and new generic medicine applications must electronically lodge their application through eBS prior to sending the hard and electronic copies of the dossier to the TGA. In this context, 'electronic lodgement' means the applicant has created an application in eBS and subsequently printed out an application form and an electronic lodgement cover sheet for inclusion in Module 1 of the dossier. Electronic lodgement, in this context, does not mean the dossier has been lodged electronically.

5.2.5 Processing the application

5.2.5.1 Effective applications

An application will be considered effective and accepted for evaluation if:

- the dossier arrives by the expected date (as identified in the Planning letter) following the lodgement of a complete PPF, and is consistent with the information in that form
- it includes the completed form: Application for the registration, or to vary the conditions of registration, of prescription medicines, or the eBS electronic equivalent (both of which include applicant declarations that all data for evaluation by the TGA has been presented at the time of dossier lodgement)
- it satisfies and is in accordance with relevant TGA regulatory requirements (see below).

5.2.5.2 TGA regulatory requirements

Applicants must abide by all applicable requirements. These requirements include, but are not limited to, those set out in:

- [Therapeutic Goods Act 1989](#)
- [Therapeutic Goods Regulations 1990](#)
- all relevant:
 - [Therapeutic Goods Orders](#)
 - [ICH and CHMP guidelines that have been adopted by the TGA](#), and other [Australia-specific guidelines](#)
- [legislative instruments](#) made under section 9D and section 23 of the Act, which encompass:
 - [Pre-submission planning form](#)
 - [Information for applicants completing a pre-submission planning form](#)

- [Application for the registration, or to vary the conditions of registration, of prescription medicines](#), or the eBS electronic equivalent
- [CTD Module 1: Administrative information and prescribing information for Australia](#)
- [Common Technical Document \(CTD\)](#)
- [Mandatory requirements for an effective application](#)

5.2.5.3 Evaluation fee

The full evaluation fee is due and payable when the applicant is notified that the application is accepted for evaluation. The Notification letter will specify the evaluation fee amount payable. If the evaluation fee for an application for the registration of a prescription medicine is not paid within two months from the date of the Notification letter, the application will lapse (see section 24(2) of the [Act](#)).

The evaluation fee amounts are available at the [fees and payments](#) section of the TGA website.

5.2.5.4 Applications not accepted

Applications that do not meet the TGA's regulatory requirements will be considered 'not effective'. Applicants of applications considered 'not effective' will be notified in writing of the reasons the application was not accepted for evaluation. If the applicant wishes to proceed with the application they must lodge a new PPF and potentially a new dossier (see section 4.2- Availability of dossier).

The dossier becomes a Commonwealth record once processing commences and cannot be returned to the applicant.

5.2.6 What happens if an applicant misses a key date?

Applicants are encouraged to contact the TGA as soon as possible if they believe that they will be unable to lodge the dossier by the expected date to allow the TGA to reallocate resources that have been assigned to the application. A revised evaluation plan will be negotiated through the relevant Case Manager.

If an application does not arrive by the expected date, the TGA will reallocate the evaluation resources assigned to that application. In such cases, the applicant will forfeit any application fee and must begin the application process with lodgement of a new PPF. If processing of the application did not commence, an applicant will be able to make arrangements to retrieve the dossier.

5.3 Phase 3: First round assessment phase

5.3.1 Objective

All data provided in the dossier are considered by the evaluators during the first round assessment phase. Where there are issues or questions about any component of the application, a consolidated section 31 request for information containing requests from all evaluation areas within the TGA is compiled and sent to the applicant by the date specified in the *Planning letter*.

Within this phase, TGA evaluators may directly contact the applicant to seek clarification or ask questions informally if they determine that waiting for the formal consolidated section 31 request on a minor clarification is unnecessary. This type of informal question will not change the timeline for the consolidated section 31 request.

5.3.2 Milestone 3

Applicants will be sent a *Milestone 3 letter* including:

- a consolidated section 31 request for information or documents, if required
- copies of the first round assessment reports prepared by the quality, nonclinical, clinical and RMP evaluators.

5.3.3 Key dates

The first round assessment phase commences the day after the *Notification letter* has been sent.

The first round assessment phase concludes 4 (generic applications) or 5 (all other applications) months later when TGA sends the applicant a *Milestone 3 letter*. This letter is sent to applicants before the end of the applicable month (or the following working day where the last day of the month falls on a weekend or [public holiday](#) in the Australian Capital Territory).

5.3.4 Assessment of data

5.3.4.1 Period for evaluation

The default timeframes for the first round evaluation of the data are:

- 3 months for the evaluation of new generic medicine applications
- 4 months for the evaluation of other applications.

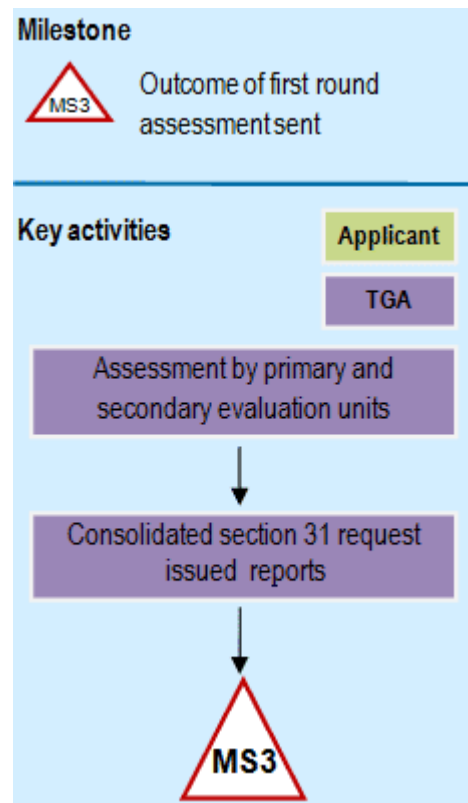
Following evaluation of the data, a consolidated section 31 request for information or documents will be compiled, checked, and authorised within 1 month of the completion of the first round assessment and sent to the applicant. This allows the TGA to ensure that issues and concerns from all evaluation areas are clearly identified and consolidated into the request.

5.3.4.2 External evaluators

The TGA may contract external evaluators to review aspects of the dossier. The TGA will coordinate the evaluation with the external evaluator as part of the first round assessment phase. Communication with the applicant in relation to an evaluation will always be through the TGA.

5.3.5 First round assessment reports

The first round assessment reports are sent with the Milestone 3 letter and will help to provide a context for any request for information or documents.



5.4 Phase 4: Consolidated section 31 request response phase

5.4.1 Objective

The consolidated section 31 request response phase allows applicants time to consider the TGA's consolidated section 31 request for information or documents, prepare a response and send the response to the TGA.

5.4.2 Milestone 4

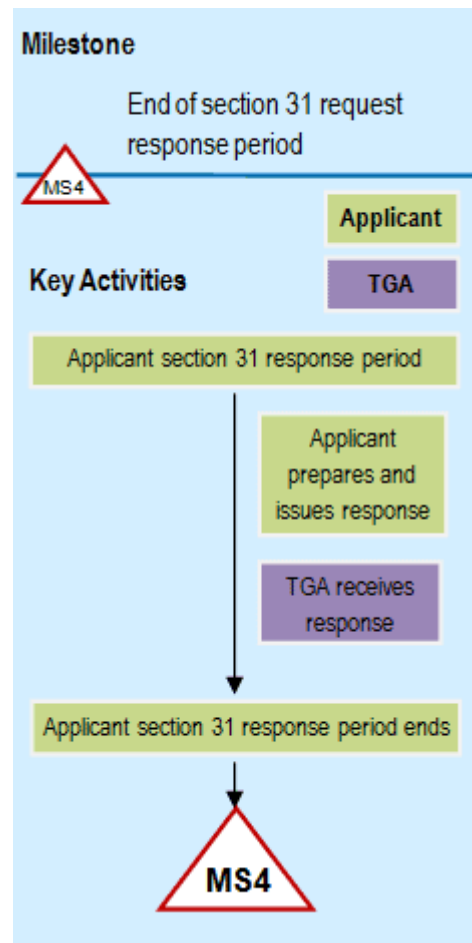
Applicants will send TGA a response to:

- any consolidated section 31 request for information or documents
- the first round assessment reports prepared by the quality, nonclinical and clinical evaluators, if required.

5.4.3 Key dates

The consolidated section 31 request response phase commences on completion of the first round assessment phase when the TGA sends the consolidated section 31 request for information or documents to the applicant.

The consolidated section 31 request response phase ends on the date by which the applicant is required to respond to the section 31 as identified in the section 31 request letter. The section 31 response time will be either 30 or 60 days as nominated by applicant in the PPF and confirmed by the TGA in the Planning letter.



Note

The consolidated section 31 request response period does not count towards the statutory 255 working day period for evaluation (Regulation 16A(2)).

5.4.4 Response to section 31 request

Responses to a section 31 request for information or documents must be provided in CTD format. Applicants need to send both hard copy and electronic copy formats of the response to the TGA. Information on providing a section 31 response is contained in [CTD Module 1: Administrative information and prescribing information for Australia](#).

Applicants should pay close attention to the questions raised in the s31 letter, as well as any requests in the letter for other information or documents, as this may be the sole opportunity that an applicant has to provide this information.

5.4.5 Response to first round assessment reports

Applicants should review the first round assessment reports and advise the TGA of any perceived errors of fact or major omissions. Each identified error of fact or omission must be

referenced to information previously submitted (Study number and location, for example, Module 3.2.P.4.3 Method validation, p.23). It is not appropriate to submit new data to negate a perceived error of fact or omission (see [Section 2.5 Information](#)). Although there is no limit to the size of an applicant's response, it is expected that the response to any one report should be no more than six single sided A4 pages and in a font no smaller than 12 point.

Responses to the assessment reports must be included in Module 1.0.2. and should be submitted with, but as separate file(s) to, the response to the section 31 request. For those applications where there is no section 31 request, applicants must respond by the date specified in the *Milestone 3 letter*. At least 14 calendar days of TGA issuing the first round assessment reports will be provided.

5.4.6 What happens if an applicant misses a key date?

The consolidated section 31 request response phase will end on the due date specified in the section 31 letter irrespective of whether an applicant's response to the request is received by the TGA.

Should the applicant not reply in the nominated time period, the second round assessment phase will be concluded based on the information available to the TGA.

5.5 Phase 5: Second round assessment phase

5.5.1 Objective

During the second round assessment phase, evaluators will consider the response provided by the applicant to the section 31 request (if applicable) and complete the evaluation of the data.

5.5.2 Milestone 5

All second round assessment reports are completed.

5.5.3 Key dates

The second round assessment phase will commence on completion of the consolidated section 31 request response phase, whether or not a response is received from the applicant.

The TGA will complete the second round assessment reports:

- within two months for applications for new generic medicines
- within one month for all other applications.

TGA will issue the second round assessment reports at the completion of the second round assessment phase.

5.5.4 Assessment of response

During the second round assessment phase evaluators consider the applicant's section 31 response to questions raised in relation to issues identified in the first round assessment. Where the section 31 response is inadequate or raises further issues, evaluators may liaise directly with applicants for clarification, but no additional time will be added and no additional section 31 requests will be formally sent. Any outstanding issues will be highlighted in the evaluation reports. These may be significant enough to warrant a recommendation to reject the application or they may be minor, possibly leading to the imposition of conditions of registration for applicant compliance.

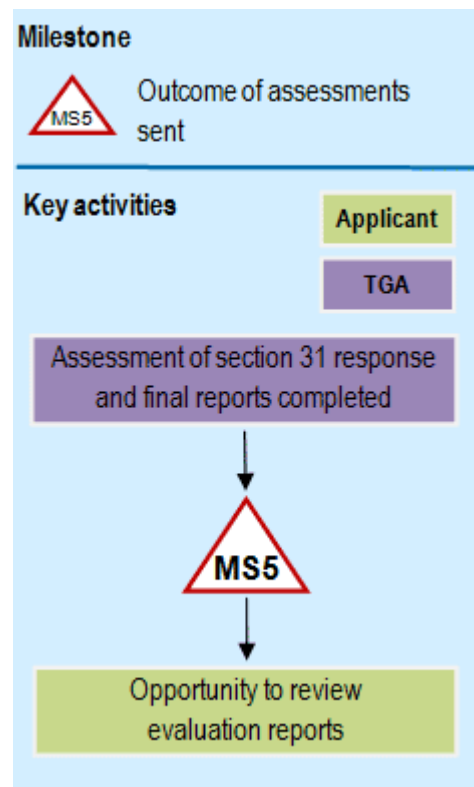
The final reports are independent assessments of the data that include advice for consideration by the decision delegate.

The TGA has no way of anticipating at the pre-submission phase whether a consolidated section 31 request will be needed or how many questions or requests for documents might be contained in such a request. Unless the TGA contacts the applicant, applicants should expect that the milestone dates identified in the Planning letter will be retained even if there is no section 31 request.

5.5.5 Opportunity to review evaluation reports

Where the application is not referred to the Advisory Committee, applicants will be given a period of 14 calendar days after the TGA issues the final evaluation report(s) in which to review and advise the TGA of any perceived errors of fact or major omissions.

Where the application is referred to the Advisory Committee, comments in relation to perceived errors of fact or major omissions in the second round assessment reports should be received by the TGA at least 13 working days before the meeting date.



5.6 Phase 6: Expert advisory review phase

5.6.1 Objective

After completion of the second round assessment phase, the evaluation reports are considered by the delegate. The delegate may seek independent advice on issues concerning the application.

The main advisory group for prescription medicines generally is the Advisory Committee on Medicines (ACM) and for vaccines specifically it is the Advisory Committee on Vaccines (ACV). Independent expert advice may also be sought by the delegate outside of the advisory committees.

Information on each of the [advisory committees](#) is available on the TGA website, including proposed meeting dates.

5.6.2 Milestone 6

The TGA notifies the applicant of the advice received from the ACM or ACV.

5.6.3 Key dates

The expert advisory review phase commences on the day the delegate's Request for ACM/ACV advice (also referred to as the Delegate's Overview for ACM/ACV) is sent to the applicant. This date is at least 23 working days prior to the proposed ACM/ACV meeting.

The Pre-ACM/ACV response from the applicant must be received by the committee secretariat at least 13 working days before the meeting date. This is to ensure that ACM/ACV have adequate time to consider the information.

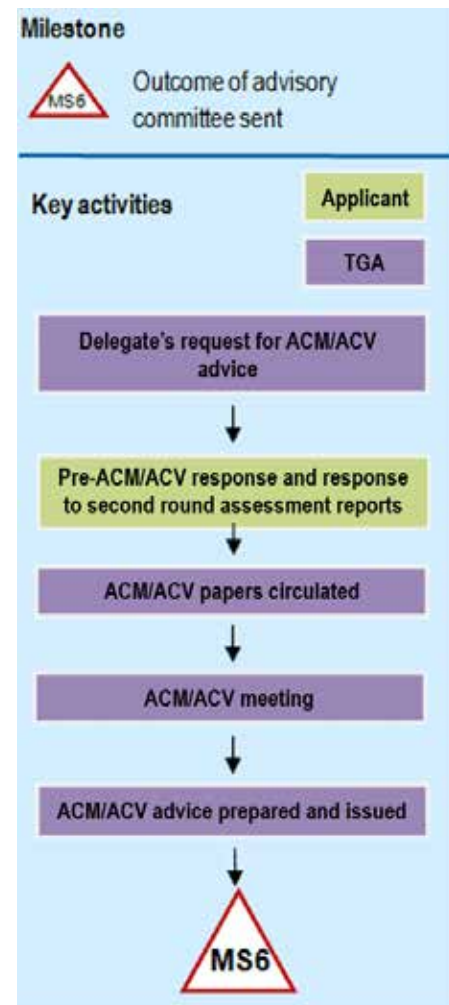
The expert advisory review phase ends when the ACM/ACV advice is sent to the applicant. This generally occurs on the Friday two weeks after the meeting (10 working days after the ACM meeting or 12 working days after the ACV meeting).

5.6.4 Advisory Committee on Medicines and Advisory Committee on Vaccines

5.6.4.1 Request for ACM/ACV advice

The delegate will review the evaluation reports and prepare a *Request for ACM advice* or *Request for ACV advice* if independent advice from the ACM/ACV is required on aspects of the application.

The delegate is not obligated to refer an application to an expert advisory committee. At the time of preparing the *Planning letter* it may not always be clear whether an application will require ACM/ACV advice; however, for applications other than those to register a new generic medicine, the *Planning letter* will identify the ACM/ACV meeting allocated to the application should the delegate decide to refer aspects of the application for advice.



When preparing the *Request for ACM advice*, the delegate will consider any outstanding issues from the evaluation process. The request contains a number of elements including:

- an overview of the application including key findings from the evaluation reports
- outstanding issues identified by the delegate
- an account of the risks and benefits relevant to the proposed product and proposed indication(s)
- a specific request for advice on any aspect of the application's characteristics, findings, or risk/benefit considerations
- whether special registration conditions, PI changes, or risk management plan changes would be appropriate.

On completion, a copy of the request is sent to the applicant prior to the ACM/ACV meeting to allow the applicant to compile a *Pre-ACM/ACV response*.

The delegate may also provide a Delegate's Overview for applications that do not require ACM/ACV advice. The purpose of this document is to summarise the evaluation and request information from the sponsor on any outstanding issues. This document will be clearly identified as not requiring ACM/ACV advice and therefore a *Pre-ACM/ACV response* will not be required. However a response addressing any outstanding evaluation issues may be required.

5.6.4.2 Pre-ACM/ACV response

The *Pre-ACM/ACV response* is the applicant's opportunity to provide comments that will be considered by the ACM/ACV. Applicants generally compile a *Pre-ACM/ACV response* based on the evaluation reports and the delegate's *Request for ACM/ACV advice*. The applicant should ensure they address any outstanding issues raised by the TGA, but should not provide new unsolicited information.

5.6.4.2.1 Guidelines for compiling the Pre ACM/ACV response

The response must be provided:

- as an electronic submission:
 - via email as a zipped attachment (maximum size 20 megabytes), or
 - on electronic media
- as an appropriately validated sequence using either the eCTD or NeeS specification, consistent with preceding sequence
- as sequence type 'Supplementary Information'; sequence description 'Pre-Advisory Committee response'
- as PDF files generated from electronically-sourced documents without placeholder documents. Include only the components that are necessary for the submission:
 - if using eCTD specification, include only 'new' documents (that is, not previously submitted in an earlier sequence)
 - if using NeeS specification, include a complete set of documents, even if previously submitted in an earlier sequence.
- with a cover letter, containing an address block, including:
Sponsor's name [or consultant's name] (as appropriate)

Return address

Attention: Regulatory affairs officer's name

Email address

Phone number

Regarding the format, the response must:

- be clearly marked '**PRE-ACM RESPONSE**' or '**PRE-ACV RESPONSE**' in bold, large upper case type at the top of the first page
- be no more than ten pages in a font no smaller than 12 point
- clearly identify upfront any changes to the indications and/or dosage and administration information from the original application.

The following should be included (as separate files) with the response:

- A tabulation of any serious unexpected adverse drug reactions which are not mentioned in the proposed Australian Product Information and have not been submitted previously – it is expected that this would normally not exceed six pages. (include under Module 1.0.3 Response to request for information).
- The updated proposed Australian Product Information and the most up-to-date Consumer Medicines Information. Please highlight changes from the version submitted with your application and reference the source of the change (e.g. clinical evaluation, company base document) in the margin. Please ensure that you comply with [Form for providing product information](#) (Module 1.3.1 Product information and Module 1.3.2 Consumer medicines information).
- A statement on the current international regulatory status of the medicine. This should detail approvals (with indications), deferrals, withdrawals and rejections (including reasons). (Module 1.11.1 Foreign regulatory status).
- Where available, provide foreign equivalent to product information (in Module 1.11.2 Foreign product information)
- A copy of the latest Periodic Safety Update Report (PSUR), unless already supplied or none is available. (Module 5.3.6 Reports of Post-Marketing Experience)

The following table provides a guide to the location of the documents in CTD format:

Pre-ACM/ACV component	CTD location*
Pre- ACM/ACV covering letter	Module 1.0.1 Cover letter
-	Module 1.0.2 Lifecycle management tracking table
Pre-ACM/ACV response	Module 1.0.3 Response to request for information
International regulatory history	Module 1.11.1 Foreign regulatory status
Adverse reactions update	Module 1.0.3 Response to request for information#

Pre-ACM/ACV component	CTD location*
Sponsor's comments on PI	Module 1.0.3 Response to request for information#
Sponsor's comments on foreign PI	Module 1.0.3 Response to request for information#
PSUR	Module 5.3.6 Reports of Post-Marketing Experience
PI (annotated and non-annotated)	Module 1.3.1.1 Product information – clean
	Module 1.3.1.2 Product information – annotated
CMI (annotated and non-annotated)	Module 1.3.2.1 Consumer medicines information – clean
	Module 1.3.2.2 Consumer medicines information – annotated
Foreign equivalent(s) to product information	Module 1.11.2 Foreign product information#

Where multiple documents are submitted in the same CTD Module, clearly identify the different documents.

More information on Pre-ACM responses is available from the ACM Secretariat at ACM@health.gov.au, and for Pre-ACV responses from the ACV Secretariat at ACV@health.gov.au.

5.6.4.3 Withdrawing a submission: AusPAR requirements

The sponsor may withdraw the submission at any time during the expert advisory review phase.

When the withdrawal letter is received by the TGA will determine whether an AusPAR is required. Refer to the [AusPAR guidance](#) for information on AusPAR business rules.

5.6.4.4 Outcome of the ACM/ACV meeting

The ACM/ACV advice is documented in the ACM/ACV 'minutes' document, which is provided to the delegate and applicant following the meeting. This generally occurs on the Friday two weeks after the meeting (10 working days after the ACM meeting or 12 working days after the ACV meeting).

The ACM/ACV advice is independent and is primarily based on their expert opinion. Note that the ACM and ACV do not make decisions and their advice does not constitute directions to the Secretary or the TGA delegate.

The ACM/ACV advice in relation to the specific questions put to the ACM/ACV is published in the [Australian public assessment report \(AusPAR\)](#). The ACM/ACV minutes may also be provided to a number of overseas regulatory agencies as permitted under section 61(4) of the [Act](#).

The ACM/ACV minutes, advice and agenda papers may also be provided to persons, bodies and authorities as permitted under section 61(5AA) of the [Act](#).

5.6.5 What happens if an applicant misses a key date?

Where the applicant cannot provide a pre-ACM/ACV response to the ACM/ACV secretariat at least two weeks prior to the meeting date, the response will generally not be tabled for consideration by the ACM/ACV, but will be considered in the decision phase by the TGA delegate. Early contact with the committee secretariat and the case manager is advised if delays are expected.

5.7 Phase 7: Decision phase

5.7.1 Objective

The TGA delegate will determine whether the application is to be approved (possibly modified or varied) or rejected. Where any outstanding issues may affect the decision, the delegate may liaise directly with the applicant during this phase before finalising the decision.

For applications made under section 23 of the [Act](#) the applicant will be notified in writing of the decision within 28 days of it being made (Section 25(4) of the Act). The issuing of a decision ends the legislated evaluation period.

5.7.2 Milestone 7

A decision is made for approval or rejection of the application for a new registration or for a variation to a registration and the decision letter is sent to the applicant.

5.7.3 Key dates

For applications referred to the ACM/ACV for advice:

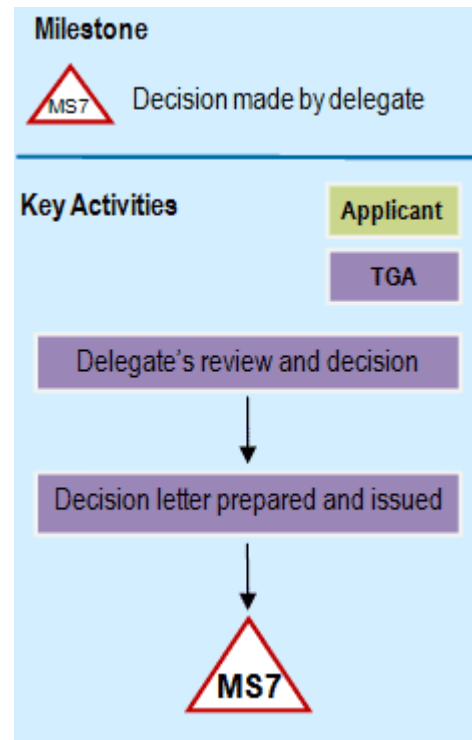
- the decision phase will commence when the ACM/ACV advice is sent to the applicant 10 working days after the Advisory Committee meeting
- the decision phase is completed when the applicant is notified of the delegate's decision 6 weeks after the ACM/ACV meeting.

For applications for new generic medicines:

- the decision phase will commence when the second round assessment reports, prepared by the relevant evaluators, are sent to the applicant
- the decision phase is completed when the applicant is notified of the delegate's decision 6 weeks after the second round assessment reports are sent to the applicant.

For other applications:

- the decision phase will commence when the second round assessment reports, prepared by the quality, nonclinical, clinical and RMP evaluators, are sent to the applicant
- the decision phase is completed when the applicant is notified of the delegate's decision 6 weeks after the ACM/ACV meeting that would have considered the application, if the application had been considered by the ACM/ACV.



5.7.4 Review and decision

5.7.4.1 Applicant's opportunity to review evaluation reports

Applicants will be given a period of 14 calendar days after the TGA issues the final evaluation report(s) in which to review and advise the TGA of any perceived errors of fact or major omissions.

Each identified error of fact or omission must be referenced to information previously submitted (Study number and location, for example, Module 3.2.P.4.3 Method validation, p.23). It is not appropriate to submit new data to negate a perceived error of fact or omission (see [Section 2.5 Information](#)). Although there is no limit to the size of an applicant's response, it is expected that the response to any one report should be no more than six single sided A4 pages and in a font no smaller than 12 point.

Responses to the assessment reports must be included in Module 1.0.2.

Applicants should also use this period to revise the draft PI based on recommendations in the evaluation reports. Please identify clearly on any revised documents:

- changes to the documents which accord fully with the recommendations of the evaluator
- changes which are partially in accord with the evaluator's recommendations, together with reasons for not fully adopting them (for example, by cross-referring to data or to the response outlining omissions or errors of fact in the evaluation)
- reasons for contesting the evaluator's recommendations
- new amendments, analogous to safety related requests, affecting safety matters.

Revised PI documents must be included in Module 1.3.1.

5.7.4.2 Delegate's review

The delegate reviews all documentation associated with the application and makes an assessment of the risks and benefits. The review may address a number of outstanding issues including suggestions for revision of the product information (PI) or risk management plan (RMP). It may also address outstanding general registration details. The delegate may negotiate issues with the applicant prior to making a decision.

5.7.4.2.1 Decision for approval

Where the delegate is satisfied that benefits sufficiently outweigh risks associated with a product, the delegate will send the applicant a decision letter for approval of a new registration (possibly varied or modified) or approval to vary a registration. There may be special conditions of registration associated with the approval; these may include the conduct of post-market activities by the applicant, or a revision of existing documentation. The decision letter will also set out the appeal rights.

5.7.4.2.2 Decision for rejection

If a delegate decides to reject an application, a formal statement of the reasons is included in the decision letter. In addition to the reasons for the decision, the letter will set out the appeal rights.

In cases where an ACM or ACV recommendation to reject an application is unexpected the delegate will usually contact the applicant to discuss the proposed actions.

5.7.5 What happens if an applicant misses a key date?

There is no obligation for an applicant to provide a response to the evaluation reports. If no response is received by TGA within the 14 calendar days period after the TGA issues the final evaluation report(s), the delegate will proceed to make a decision based on the available information.

Applicants are responsible for monitoring existing GMP clearances that may be due to expire prior to or during the decision phase. A delegate is unable to approve an application for a new registration unless:

- all Australian manufacturer(s) involved hold a valid licence for the relevant production steps
- all overseas manufacturer(s) involved hold a valid GMP clearance for relevant production steps.

5.8 Phase 8: Post-decision phase

5.8.1 Objective

During the post-decision phase, administrative and regulatory activities are completed.

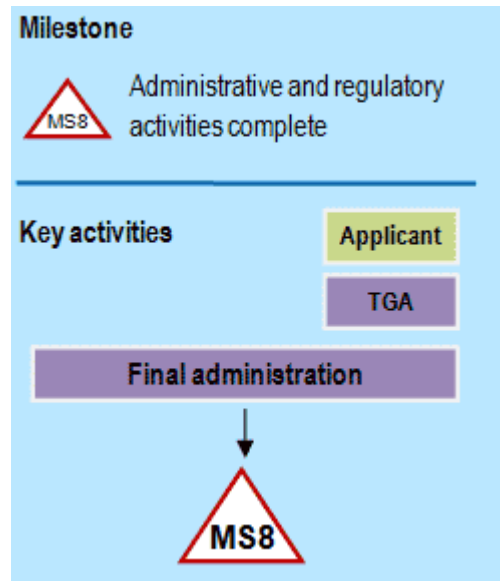
5.8.2 Milestone 8

Administrative and regulatory activities are completed. Any outstanding payments are finalised (if applicable) and the ARTG entry is finalised.

5.8.3 Key dates

The post-decision phase commences when the applicant is notified of the delegate's decision.

The post-decision phase is completed by the end of the month following the delegate's decision.



Note

If an appeal is lodged prior to milestone 8, the milestone will be delayed until all appeal activities are complete. Under section 60 of the Act, an appeal by the applicant must be lodged within 90 days of notification of the decision.

5.8.4 ARTG registration

A new Register entry³ can only be included on the ARTG once the applicant provides a patent certificate or notice (section 26B(1) of the Act) to the TGA (see section 25(4) of the Act).

The TGA will check that the provisional ARTG record (originally provided by the applicant at dossier lodgement and updated during evaluation) matches the approved product details. The provisional ARTG record will become the ARTG Record of Registration.

The applicant must notify the TGA of the actual date of marketing commencement and meet other conditions of registration outlined in the delegate's decision letter.

5.8.5 Medicines information

After registration medicines information about the product and the decision process will be made available to the public through the TGA website. This information will be published as:

- an Australian Public Assessment Report (AusPAR)

³ A new registration (or new Register entry) is one that requires a new ARTG entry by reason of being 'separate and distinct goods' under s.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, and extensions of indication. However, not all new registrations will result in the allocation of a new AUSTR number if they are taken to be grouped by reason of the Therapeutic Goods (Groups) Order 2001.

The AusPAR provides information about the evaluation of a prescription medicine and the considerations that led the TGA to approve or not approve an application. The AusPAR is drafted during the post-decision phase and sent to the applicant for review prior to publication on the [TGA website](#). Details of the contents, rules, and activities associated with an AusPAR are provided in [Australian public assessment report for prescription medicines guidance](#), accessible on the TGA website.

- an Australian Prescription Medicine Decision Summary

The Australian Prescription Medicine Decision Summary provides a short overview of the TGA's evaluation process leading to the registration of a new prescription medicine on the ARTG. Australian Prescription Medicine Decision Summaries are drafted during the post-decision phase and published on the [TGA website](#).

- product information (PI)

Product information document(s) in the approved form must be lodged by the applicant with the TGA within 2 weeks of the date of registration of the product(s).

- consumer medicines information (CMI)

- CMI document(s) must be lodged with the TGA:

- § for new product(s) - prior to first supply of the product(s)







- § for variations to existing products - within 2 weeks of the date of approval of the variation.

5.8.6 What happens if an applicant misses a key date?




The post-decision phase for new register entries cannot be completed unless the section 26B(1) Certificate required in relation to patents is provided by the applicant.

Appendix 1 - Sample timelines

New Chemical Entity









Activity	Date	Milestone
Pre-submission phase		
Applicant submits pre-submission planning form	30 Nov 2012	
TGA commences processing PPF	1 Dec 2012 (3 Dec 2012*)	
TGA <i>Planning letter</i> issued	On/before 15 Jan 2013	 MS1
Submission phase		
Applicant lodges dossier	On/before 7 Feb 2013	
TGA <i>Notification letter</i> issued	On/before 28 Feb 2013	 MS2
First round assessment phase		
Commencement of evaluation	1 Mar 2013	
Consolidated section 31 request sent from TGA to applicant	On/before 31 Jul 2013	 MS3
Consolidated section 31 request response period		
30 day option - selected at PPF	On/before 30 Aug 2013	 MS4
60 day option - selected at PPF	On/before 29 Sep 2013 (30 Sep 2013*)	 MS4
Second round assessment phase (assuming 30 day response period)		
Completion of second round assessment	On/before 30 Sep 2013	 MS5

Planned evaluation time is 10.5 months

Activity	Date	Milestone
Expert advisory review phase (assuming submission referred)		
Request for ACM advice sent to applicant	5 Nov 2013	
Pre-ACM response received	19 Nov 2013	
ACM meeting	6 Dec 2013	
ACM advice finalised	20 Dec 2013 (23 Dec 2013*)	 MS6
Decision phase		
Decision date	On/before 15 Jan 2014	 MS7
Post-decision phase		
ARTG entry created	On/before 15 Feb 2014 (17 Feb 2014*)	 MS8

*Where the target date falls on a weekend or public holiday, the actual target date will be the next working day.

Generic medicine

Activity	Date	Milestone
Pre-submission phase		
Applicant submits pre-submission planning form	31 Oct 2012	
TGA commences processing PPF	1 Nov 2012	
TGA <i>Planning letter</i> issued	On/before 15 Dec 2012 (17 Dec 2012*)	
Submission phase		
Applicant lodges dossier	On/before 15 Jan 2013	
TGA <i>Notification letter</i> issued	On/before 31 Jan 2013	
First round assessment phase		
Commencement of evaluation	1 Feb 2013	
Consolidated section 31 request sent from TGA to applicant	On/before 31 May 2013	
Consolidated section 31 request response period		
30 day option - selected at PPF	On/before 30 Jun 2013 (1 Jul 2013*)	
60 day option - selected at PPF	On/before 30 Jul 2013	
Second round assessment phase (assuming 30 day response period)		
Completion of second round assessment	On/before 31 Aug 2013 (2 Sep 2013*)	
Decision phase		
Decision date	On/before 15 Oct 2013	
Post-decision phase		
ARTG entry created	On/before 15 Nov 2013	

Planned evaluation time is 8.5 months

*Where the target date falls on a weekend or public holiday, the actual target date will be the next working day.

Appendix 2 - Registration process regulatory phases

Phase	Pre-submission	Submission	First round assessment	Consolidated section 31 request response	Second round assessment	Expert advisory review	Decision	Post-decision
Milestone	MS1 Outcome of pre-submission planning sent	MS2 Outcome of submission consideration sent	MS3 Outcome of first round assessment sent	MS4 End of s.31 request response period	MS5 Outcome of assessments sent	MS6 Outcome of advisory committee sent	MS7 Decision made by delegate	MS8 Administrative and regulatory activities complete
Major activities	PPF lodged before first of month Pre-submission planning	Dossier arrives at TGA by COB 7th or 14th of month (unless applicant advised of alternative date) Processing and considering submission	First round assessment Consolidated section 31 request compiled	Applicant preparation of response to section 31 request and first round assessment reports Response received by TGA or response period ends	Second round assessment	Advisory committee meeting Pre-ACPM response and review of reports Delegate overview Committee advice prepared Committee papers circulated	Delegate decision including PI/CMI/RMP negotiation	AusPAR C-i-C content review and PI/CMI requirements fulfilled Documents published, new/ revised ARTG entry
Regulatory requirements	PPF and attachments lodged via eBS. Only PPFs lodged before first of month processed. PPFs that are not complete will be considered not acceptable. Applicants who have lodged complete PPFs will receive <i>Planning letter</i> outlining: - submission milestones - feedback from TGA on justifications or other aspects affecting application - any specific conditions for dossier lodgement. Pre-submission meetings are voluntary and not linked to PPF lodgement. They may occur at any stage prior to dossier lodgement and are recommended for complex applications or special cases.	Applications must be received by the TGA by COB 7 th or 14 th of the month unless otherwise advised in <i>Planning letter</i> . Applicants must certify that all information has been presented at the time of dossier lodgement. Only information requested by the TGA in a s.31 request or safety related data can be supplied after dossier lodgement. The TGA will process and consider submission dossiers against regulatory requirements. Applications not provided in accordance with regulatory requirements will be considered not effective and not accepted for evaluation. Applicants will receive a <i>Notification letter</i> advising whether the application has been accepted or not accepted for evaluation.	All dossier content is evaluated during this phase. Draft evaluation reports are prepared. If required, a consolidated s.31 request for information will be prepared. This includes requests from all evaluation units. This request is compiled in the final month of the phase and sent to the applicant on the date specified in the <i>Planning letter</i> .	Applicants nominate in the PPF whether they will respond to the request in 30 or 60 calendar days. The MS3 date is confirmed in the <i>Planning letter</i> . If applicants do not respond to a request for information by the date identified in the <i>Planning letter</i> , evaluators complete the evaluation based on the information provided in the dossier at dossier lodgement. Applicants have opportunity to review the first round assessment reports for factual content.	Evaluators consider the section 31 response (if applicable) and finalise the evaluation reports. Where evaluators identify outstanding issues, they will be presented in the evaluation reports for consideration by the delegate.	Where the delegate seeks independent advice on aspects of an application, the delegate prepares a request for advice letter. New innovator products, new indications, and complex applications will generally be referred to the ACPM. The applicant will have an opportunity to prepare a pre-committee response addressing issues raised in the delegate's request for advice letter. Applicants have an opportunity to review the second round assessment reports for factual content. Committee advice is finalised and sent to the applicant on the 15 th of the month of the meeting.	The delegate will generally informally advise the applicant of the decision. Formal correspondence of the decision is sent to the applicant. If the delegate proposes to approve an application, prior to approval, any outstanding issues relating to PI, CMI, or RMPs may be negotiated with the applicant. Approval may be conditional on resolution of issues. If the delegate proposes to reject an application, the reasons for the decision are included in the letter of decision, with an explanation of appeal rights.	Registration of a new product or variation to a register entry completed. For applicable application types, a draft AusPAR will be compiled.

Version history

Version	Description of change	Author	Effective date
V1.0	First version	Office of Prescription Medicines	02/2010
V2.0	Second version to reflect outcomes from the public and stakeholder consultation, the introduction of a separate workflow for generic medicines and the opportunity for applicants to consider all evaluation reports at milestone 3	Office of Prescription Medicines	05/2013
V2.1	Addition of link to guidance on orphan drug designations	Office of Medicines Authorisation	09/09/2014
V2.2	Update to reflect new legislation	Prescription Medicines Authorisation Branch	01/07/2017
V2.3	Updated to reflect Provisional approval pathway	Prescription Medicines Authorisation Branch	20/03/2018
V2.4	Minor updates to Submissions	Prescription Medicines Authorisation Branch	August 2020

Version	Description of change	Author	Effective date
V2.5	<p>Updates to expert advisory review phase</p> <ul style="list-style-type: none"> • Use of the phrase ACM/ACV rather than only ACM • Provide additional details regarding the Pre-ACM/ACV responses (within 5.6.4.2) • Update timeframes for provision of ACM/ACV minutes in line with current practice (within 5.6.3 & 5.6.4.4) • Removal of the Pharmaceutical subcommittee information • Expectation for reviewing evaluation reports combined for both applications that attend ACM/ACV and that do not attend ACM/ACV (within 5.7.4.1) • Inclusion of information about Decision Summaries (within 5.8.5) • Minor edits to increase readability 	Prescription Medicines Authorisation Branch	August 2021

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 #