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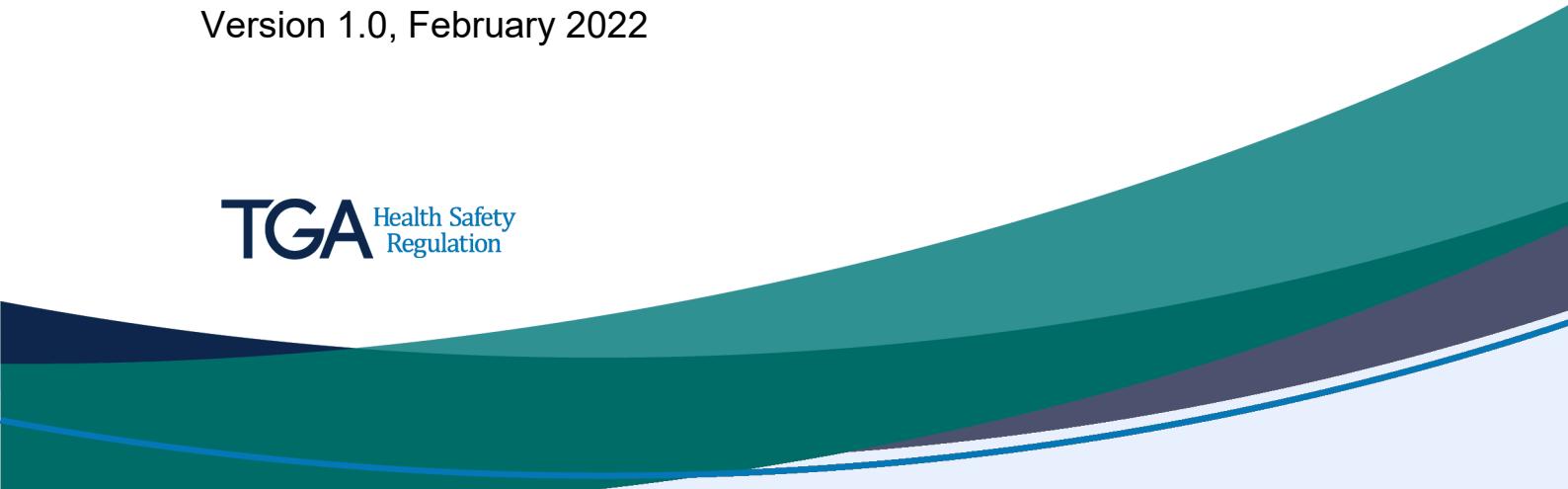
Therapeutic Goods Administration

Priority Review pathway for biologicals: feasibility, potential eligibility criteria and determination process

Consultation paper

Version 1.0, February 2022

TGA Health Safety
Regulation



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Purpose and scope

The introduction of a priority pathway for biologicals was advocated by several submissions to the recent [House of Representatives Inquiry](#) into approval processes for new drugs and novel medical technologies in Australia, and in feedback from stakeholder interviews conducted by MTP Connect as part of a review commissioned by the TGA on regulation of gene, cell and tissue therapies.

Subject to wider stakeholder views from this consultation, the Therapeutic Goods Administration (TGA) could propose to the Government that a priority pathway be implemented for the pre-market assessment and registration of novel biologicals that address unmet clinical needs for Australian consumers. This would require changes to the [Therapeutic Goods Regulations 1990](#).

Biologicals include human cell and tissue (HCT) therapies and viable animal cell and tissue therapies. A **Priority Review** pathway would offer a faster formal assessment pathway for biologicals in certain circumstances. This pathway would allow consumers with life-threatening diseases or seriously debilitating conditions to access these treatments in less time, where the assessment results in a decision by the TGA to include the biological in the [Australian Register of Therapeutic Goods \(ARTG\)](#). With industry poised to deliver more late-stage clinical and commercial biologicals for such illnesses with high unmet medical need, bringing such products to patients through optimised regulatory and expedited pathways is crucial.

The purpose of this consultation paper is to provide an opportunity for consumers, healthcare professionals and industry to provide advice to government on a **Priority Review** pathway for biologicals, specifically:

- whether they **support introduction** of such a pathway
- **eligibility criteria** for the Priority Review pathway for biologicals
- the **Process** for determining whether a biological application meets the eligibility criteria for Priority Review (the 'Determination Process').

This consultation focuses on how a Priority Review pathway could apply to biologicals. We will work with industry to develop business processes and guidance documents to support the implementation of this new pathway. In 2016, TGA conducted a [public consultation](#) focusing on expedited review for prescription medicines that stated the new pathway could potentially also be applied to biologicals as part of future considerations. Soon after, a Priority Pathway was established by government for prescription medicines (see below).

Principles for Priority Review

We are applying the following principles to guide the proposed development of a Priority Review pathway for biologicals:

- The quality, safety and efficacy of therapeutic goods must be maintained to assure the continued confidence in TGA's regulation by the healthcare professional and the consumers.
- TGA will provide clear guidance to enable applicants to adhere to the determination¹ and registration processes².

¹ By 'determination process', we are referring to a formal process which will occur before a sponsor makes an application for inclusion of a biological in the ARTG. The determination process will identify whether a biological is eligible for the Priority Review pathway but does not necessarily mean that the biological will be approved after evaluation by TGA.

² By 'registration process', we are referring to the process of evaluating an application and making a decision about whether to include a biological in the ARTG.

- Applicants will be responsible in providing TGA with all necessary information in order to receive, and support, continued fast track status via Priority Review.
- Both TGA and applicants will commit to open and timely communication to support expediting the application in the interests of public health.
- There will be transparency in the criteria for Priority Review, and of determination and registration decisions, although it is proposed that only positive determination decisions would be published.
- A legislated timeframe would apply for review of those products given priority review.
- The determination and registration processes will be cost-recovered.
- Appeal rights regarding determination decisions will be in place.

Background

Biologicals framework

[The regulatory framework for biologicals](#) commenced in May 2011 and provides the legislative basis for the regulation of HCT-derived products and live animal cells or tissues that are supplied in, or exported from, Australia. The framework applies different levels of regulation to products based on the risks associated with their use. It is designed to be flexible enough to accommodate emerging technologies.

Since the introduction of the biologicals framework there has been no formal mechanism to expedite the assessment and inclusion of biologicals in the ARTG. In circumstances where a therapeutic good is considered by TGA to be a significant therapeutic advance or of critical importance to the Australian community, we have worked with relevant sponsors to facilitate early access to the new product, provided that it meets the TGA's quality, safety and efficacy requirements. A priority pathway will provide a predictable and transparent mechanism to formalise these processes for sponsors and TGA business areas.

Context for change

As noted above, calls from industry and clinician and patient groups for an expedited pathway for the assessment of biologicals have been made through different fora. Furthermore, current TGA assessment practices for expedited review of applications for biologicals are inconsistent with those of other therapeutic goods and equivalent overseas regulators. For example, both the FDA and EMA have programs that facilitate the truncation of assessment timeframes for products equivalent to [biologicals](#) (see [Appendix 1](#)).

Objectives of a priority pathway

The objectives of a priority pathway are to:

- assist in achieving a faster assessment and earlier access to certain novel and life-saving biologicals that address unmet clinical needs for Australian consumers, bringing these to market faster than using standard evaluation pathways

- provide timely and flexible registration processes for sponsors seeking access to the Australian market for new and novel uses of biologicals that offer substantial benefits to Australian consumers
- increase alignment with other overseas regulators that offer accelerated assessment processes.

The **Priority Review** pathway will prioritise the evaluation of novel biologicals that meet the eligibility criteria and have a **full dossier**, with a view to reducing the target timeframe for a decision regarding inclusion of the biological in the ARTG. A **legislated timeframe of 150 working days** is proposed for Priority Review,³ which is consistent with benchmarks set by EMA and US FDA for similar programs, and the Priority Review pathway for prescription medicines used by TGA.

The Priority Review pathway for biologicals will require new and flexible business processes to facilitate faster assessment for registration, while maintaining our high standards for quality, safety and efficacy.

Eligibility for Priority Review pathway

In drafting the proposed eligibility criteria for the Priority Review pathway for biologicals, consideration has been given to the criteria for equivalent pathways administered by TGA for [prescription medicines](#) and [medical devices](#). Consideration has also been given to the criteria for equivalent programs administered by international regulators including EMA and US FDA.

While there are no standard criteria for priority pathways for biologicals, there are some common considerations, namely the:

- seriousness of the disease or condition and its impact on people's daily lives
- existence of effective interventions
- extent of (potential) innovation offered by the product, that is, whether the treatment will provide a substantial benefit in some aspect of the patient outcomes.

Although the criteria are principles-based, fulfilling them will require an analysis of data.

Proposed criteria for acceptance of an application

The eligibility criteria for Priority Review determination are designed to ensure that only biologicals providing the most benefit to patients are eligible. Priority Review is based on a **full dossier of data**. Priority Review is intended for biologicals that represent a major advantage over existing treatments available to Australian patients.

There are **four criteria** proposed for the Priority Review pathway for biologicals. **All these criteria must be satisfied** for a biological to be eligible for Priority Review. A delegate of the Secretary, in practice a senior medical officer of the TGA, will determine the validity of the justifications against the eligibility criteria on a case-by-case basis. As part of the routine determination process, the extent to which criteria are met will be assessed at the time a decision is made on the application.

³ As opposed to the current legislative timeframe of 255 working days for 'standard' biologicals applications (*Therapeutic Goods Regulations 1990*).

Criterion 1: New biological or new use

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The biological is either a **new biological** or an **already registered biological with a new use**.

Only certain types of biologicals are eligible for Priority Review determination. The biological must be either a new biological or an already registered biological with a new use.

A new biological contains:

- An active ingredient that has not previously been included in an entry in the ARTG; or
- A fixed combination of biological, chemical or radiopharmaceutical active ingredients, or device, at least one of which has not previously been included in an entry in the ARTG.

A new use biological:

- Has the same active ingredient (or fixed combination of such ingredients) as another therapeutic good included in the ARTG; and
- Does not have the same use (encompassing either ‘intended use’ [for Class 1 and 2 biologicals] or ‘therapeutic indication’ [for Class 3 and 4 biologicals]) as that other biological.

Criterion 2: Life-threatening disease or seriously debilitating condition

Criterion 2: Life-threatening disease or condition

The biological is to be used for the treatment, prevention or diagnosis of a **life-threatening disease** or **seriously debilitating condition**.

To ensure the Priority Review pathway benefits patients in need of vital and life-saving biologicals, the biological must be used for the treatment, prevention or diagnosis of a **life-threatening disease** or **seriously debilitating condition**.

The severity of the disease in Australia (i.e., its life-threatening or seriously debilitating nature) needs to be justified based on objective and quantifiable medical information. The determination application must justify the nature of the disease or condition **based on figures of morbidity or mortality and life expectancy** in Australia.

- A [life-threatening condition](#) is defined by TGA as one where the prominent feature (i.e. affecting an important portion of the target population) is a serious illness from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of treatment based on mortality and life expectancy data.
- A [seriously debilitating condition](#) is defined by TGA as one that has as a prominent feature (i.e. affecting an important portion of the target population) which is morbidity with a well-established, major impact on the functioning of the person based on objective and quantifiable medical or epidemiologic information. Short-lived and/or self-limiting morbidity is not considered seriously debilitating.

The potentially fatal or debilitating outcome should be a prominent feature of both the target disease or condition and use (either intended use or therapeutic indication), i.e., affect an important portion of the target population.

Criterion 3: Fulfils an unmet clinical need or clinically significant improvement over already approved therapeutic goods

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Either:

- No therapeutic goods that are intended to treat, prevent or diagnose the condition are entered on or included in the ARTG; or
- If one or more therapeutic goods that are intended to treat, prevent or diagnose the condition are entered on or included in the ARTG—there is **substantial evidence demonstrating** that the biological provides a **clinically significant improvement** in the safety or efficacy of the treatment, prevention or diagnosis of the condition **compared to** those goods.

Sponsors and manufacturers must review therapeutic goods entered on or included in the ARTG for diagnosis, prevention or treatment for the proposed use in Australia, and provide:

- Details of any registered therapeutic goods for diagnosis, prevention or treatment of the disease or condition in question; and
- Either:
 - A declaration that there are no therapeutic goods in Australia in accordance with ARTG entries at the date of determination application lodgement; or
 - A justification demonstrating **substantial evidence** for a **clinically significant improvement** in safety or efficacy when **compared to** already registered therapeutic goods; and
- A justification that the new use (intended use or therapeutic indication) should be considered if the biological is already registered for a similar condition.

Sponsors and manufacturers must describe how and to what extent the biological is expected to fulfil an unmet medical need if there are no already approved therapeutic goods or that it provides a clinically significant improvement with reference to the therapeutic goods registered for the indicated population, the importance of the effects of the proposed biological, and the benefit of the proposed biological.

Already approved therapeutic goods

In reviewing therapeutic goods already on the ARTG, sponsors and manufacturers should consider all goods including medical devices. Sponsors and manufacturers must provide an overview table of trade names, identifying numbers (e.g., AUST numbers), the holders of the ARTG entry, and the use. Some older, already approved products can have especially broad uses for a number of diseases or conditions, so please conduct your review carefully to identify if there is an unmet clinical need.

Any reference to an already approved therapeutic good must be limited to the conditions of the relevant entry. Therefore, a biological that is administered or applied outside the approved

product information ('off-label' use) cannot be considered an existing therapeutic good. [Provisionally registered](#) goods in the ARTG are also excluded from this comparison.

Clinically significant improvement in safety or efficacy

It must be demonstrated that there is **substantial evidence** that the biological provides a **clinically significant improvement** when **compared to** already approved therapeutic goods for the use (intended use or therapeutic indication) that is the subject of the determination application (for treatment, prevention or diagnosis of the condition) by addressing either of the following:

- a better safety profile for the entire population relevant to the use; or
- improved efficacy for the entire population relevant to the use.

If new goods for the diagnosis, prevention or treatment of a proposed use are entered on or included in the ARTG after sponsors and manufacturers lodge their application, they will have the opportunity to submit a further justification of clinically significant improvement in safety or efficacy in relation to those goods before a determination decision is made on their application.

Supporting evidence should be based on clinical trial data. Increased safety or efficacy should be demonstrated through established safety and efficacy endpoints that demonstrate direct clinical benefit.

Comparator studies are expected to be generated (pivotal study reports). TGA will not assess clinically significant improvement against comparators that are a subject of concurrent determination or registration application. [Provisionally registered](#) goods in the ARTG are also excluded from this comparison.

For a claim of improved safety or efficacy, TGA will evaluate whether there is a high probability that patients will experience a clinically relevant benefit. Therefore, this claim must be supported by robust evidence from summaries of full study reports that form the basis of the intended registration application, and justifications presented by the sponsor.

The data must be considered in light of the particular characteristics of the condition (e.g., life expectancy, symptoms) and the registered biologicals for the treatment, prevention or diagnosis of the proposed use.

Criterion 4: Major therapeutic advantage

Criterion 4: Major therapeutic advantage

There is **substantial evidence demonstrating** that the biological provides a **major therapeutic advantage in patient outcomes** when **compared to** existing treatments as defined by a **magnitude well beyond the minimum threshold of clinical significance**.

A [major therapeutic advance](#) is defined by TGA as an improvement in the safety and/or efficacy of the medicine that is of a magnitude well beyond the minimum threshold of clinical significance. The impact on patient outcomes for the indicated population will consider effects on both safety and efficacy. The magnitude of the demonstrated improvement in safety and/or efficacy will be assessed in relation to existing treatments for the relevant disease or condition.

Your determination application must provide a justification that there is **substantial evidence** that the biological is a **major therapeutic advance** based on the following aspects:

- The magnitude of the demonstrated improvement in safety and/or efficacy.

- The impact on patient outcomes considering both safety and efficacy.
- Endpoints that directly demonstrate clinical benefit (e.g., overall survival [OS] and progression-free survival [PFS] for oncology-based biologicals).
- The magnitude of the advance in relation to other therapeutic goods registered for the indicated population:
 - where no product is on the ARTG, the comparison should occur against the standard of care.
- The strength of evidence.

Sponsors and manufacturers must include an assessment of the **magnitude** of the demonstrated improvement in safety or efficacy based on established safety and efficacy endpoints.⁴ The demonstration of a biological's clinically significant benefit based on improved safety and/or efficacy is not sufficient. Rather, there should be **demonstration of a major benefit**, i.e., well beyond the level that could be described as clinically significant (e.g. a major improvement in mortality endpoints). Even if the benefit appears in one aspect only, sponsors and manufacturers must assess the overall impact on patient outcomes considering both safety and efficacy. Patient-reported outcomes may be provided, but these are not a universal requirement (depending on the setting).

The description of the strength of evidence should include a brief outline of the main available evidence (e.g., number and type of clinical trials with clear delineation of pivotal versus supporting studies, sample size, design and key results) on which the claim is based.

A biological that demonstrates clinically significant improvement in safety or efficacy (Criterion 3) may constitute a major therapeutic advance (Criterion 4) if, for example, the biological demonstrates cure rates that are higher than those observed in previous treatment options, while also replacing a standard treatment that has poor tolerability and potential for serious side effects.

Examples of applications that are not Priority

Following TGA's experiences in assessing Priority determinations for prescription medicines, examples of applications that would likely be refused a Priority determination for biologicals include the following:

- The active ingredient has already been included in an entry in the ARTG (Criterion 1).
- The condition is not life-threatening nor seriously debilitating (Criterion 2).
- There are therapeutic goods that are intended to treat, prevent or diagnose the condition already included in the ARTG, and there is no substantial evidence demonstrating the biological provides a clinically significant improvement in the safety or efficacy of the treatment, prevention or diagnosis of the condition compared to those goods (Criterion 3).
- There is insufficient evidence demonstrating the biological provides a major therapeutic advantage (Criterion 4) based on the:
 - magnitude of clinical benefit compared to placebo and/or existing therapies
 - incidence of adverse reactions compared to placebo and/or existing therapies

⁴ Use of international benchmarks or guidance from international bodies such as the European Society for Medical Oncology (ESMO) and Magnitude of Clinical Benefit Scale (ESMO-MCBS) are encouraged for justifying clinical efficacy.

- quality of the evidence in support of a benefit, i.e., a small study.



Question 1: Do you support introduction of a priority pathway for biologicals?

Question 2: Is there any expected impact if the proposed Priority Review pathway was to be implemented?

Question 3: Do you agree that the 4 proposed criteria for Priority Review of biologicals address the objectives of an expedited pathway?

Question 4: Do you believe any eligibility criteria should be added, amended, or removed from the proposed Priority Review pathway?

Determination for Priority Review pathway

Determination process

Subject to the implementation of a priority review pathway by government, the TGA would introduce a formal determination process for deciding whether a biological is eligible to enter the Priority Review pathway. In line with the approach for other expedited pathways (prescription medicines and medical devices), sponsors will be responsible for providing TGA with all the information necessary to receive and support continued determination for the Priority Review pathway.

The steps in the determination process are summarised in Figure 1.

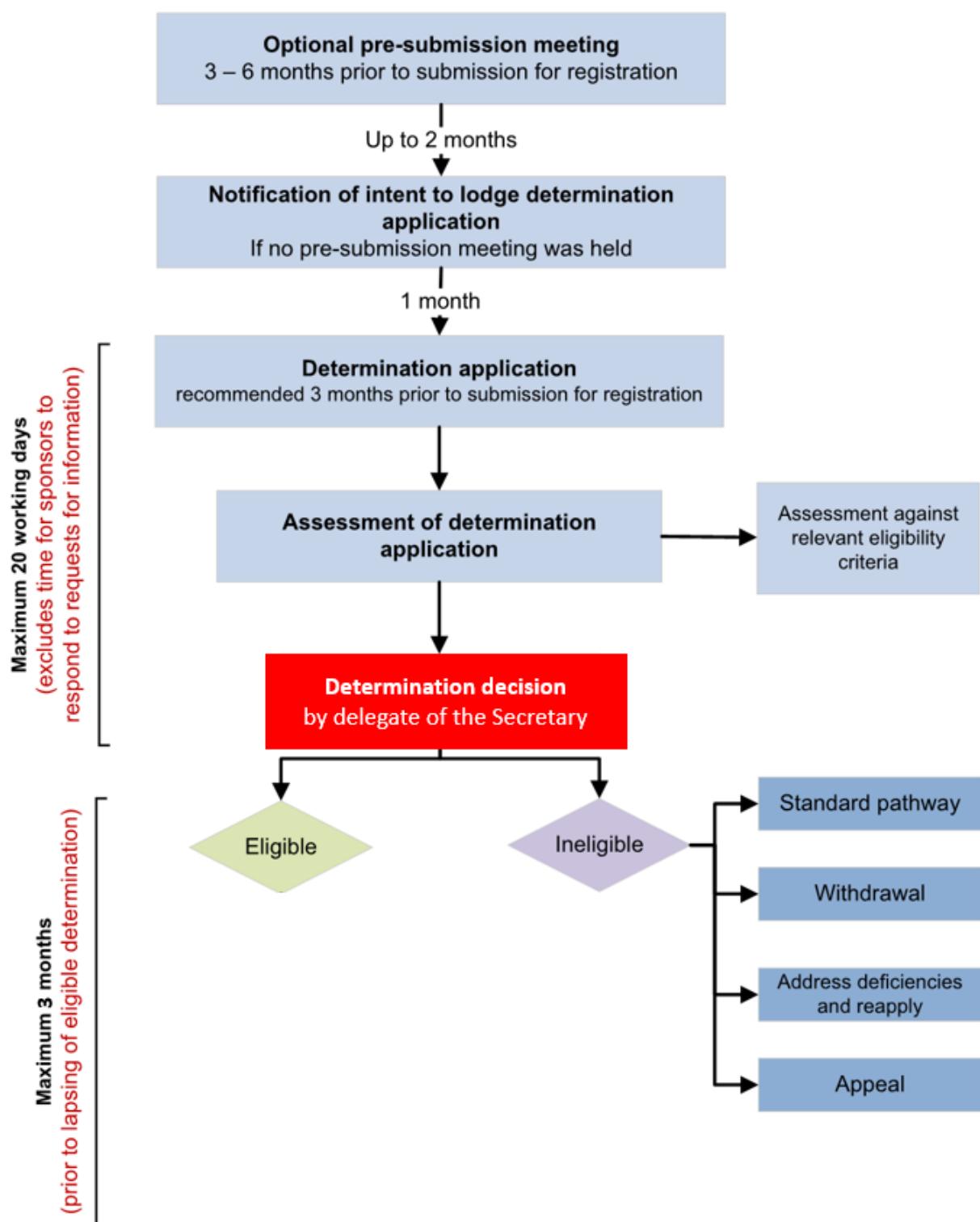


Figure 1: Determination process for Priority Review pathway for biologicals.

Optional pre-submission meeting

Pre-submission meetings will be recommended for sponsors intending to apply for determination to the Priority Review pathway. It is proposed that pre-submission meetings will occur approximately 3-6 months prior to submission of the dossier for the registration process. This early indication will provide sponsors with an opportunity to clarify any details relating to their application, including relevant Good Manufacturing Practice (GMP) requirements. It will also provide TGA with an early indication of resource and expertise needs for the determination and registration processes.

Notification of intent to lodge determination application

Pre-submission meetings may not be needed for all applications since this information could also be gathered through phone or e-mail communication.

If there is no pre-submission meeting, there is an option for sponsors to submit a notification of intent to lodge a determination application approximately one month beforehand.

Determination application

It is proposed that an application for determination for Priority Review should be submitted to TGA approximately three months prior to submission of the dossier for the registration process.

Assessment of determination application

It is proposed that sponsors will submit an application form seeking determination for Priority Review and provide a rationale as to why their biological meets the eligibility criteria. Sponsors will be responsible for providing all information necessary to receive and maintain the determination.

Sponsors will need to provide current evidence that their GMP licence, certificate or clearance for manufacturers (including overseas manufacturers) includes all steps in manufacture or preparation covering the proposed Priority Review application. If applying for GMP clearance, compliance evidence will be required prior to the determination decision.

Determination decision

Within TGA, the relevant delegate of the Secretary will assess the information provided by the sponsor against the criteria to decide whether a biological should be granted a determination for the Priority Review pathway. It is proposed that the delegate will have a **target timeframe of 20 working days** from acceptance and acknowledgement to the sponsor of a complete application to make the decision.

Note that should further information be sought from a sponsor by TGA, a **clock stop** will be initiated, with the determination time restarted when responses are supplied.

The delegate of the Secretary may consult internally with TGA clinical delegates, medical officers and legal support to inform their determination decision, and may also seek advice from external experts. The delegate of the Secretary as the sole decision maker for determination decisions gives consistency to the decision-making. The [Advisory Committee for Biologicals \(ACB\)](#) will be regularly informed of determination decisions from the Priority Review pathway.

Successful determination of an application as Priority Review does not mean that the biological will be approved after evaluation and included in the ARTG. Applications that are decided as being ineligible for Priority Review may still apply for registration via the [standard biologicals pathway](#).



Question 5: Do you agree that the proposed determination process and timing of the steps is appropriate?

One biological, one use

The application for Priority Review determination is specific to the applicant, the product and use. The determination for Priority Review therefore **applies to a specific biological for a specific use**, with applicants only able to apply for only **one biological and one use** in a Priority Review determination application.

If determination for multiple uses is required, one application must be submitted for each; there is no bundling of uses for Priority Review. A registration submission that is a combination of Priority and non-Priority will not be eligible for review under the Priority Review pathway.

The proposed use at the time of determination may be different to that approved at the time of registration as a result of the assessment of the quality, safety and efficacy data submitted with the registration application.

Combinations of biologicals and/or medicines that are not fixed dose combinations require separate applications (one for each component of the non-fixed dose combination).

Classes of biologicals

The Priority Review pathway is proposed to apply for **biologicals** that are **either**:

- Class 4: high risk
- Class 3: medium risk
- Class 2: low risk.

It is proposed that the following biologicals **will not be able to apply** for Priority Review:

- Class 1: low risk and have an appropriate level of external governance and clinical oversight.

Classification is generally determined by the level of processing applied to the biological (method of preparation, including whether minimally manipulated), the intended use of the product, and the level of external governance and clinical oversight.

An example of a Class 1 product is a faecal microbiota transplant (FMT) product that is manufactured within a hospital setting.

Appeals

Sponsors will be able to seek internal review of the Priority Review determination decision under section 60 of the *Therapeutic Goods Act 1989* or external review from the Administrative Appeals Tribunal. Appeal rights will be consistent with TGA's transparency and accountability obligations, and existing appeal timeframes will apply.

Biovigilance

As with 'standard' biologicals applications for inclusion in the ARTG, those biologicals applications determined eligible for Priority Review must have a robust [biovigilance system](#) in place.

Duration of determination

It is proposed that after a determination for Priority Review has been positively granted by TGA, the sponsor will be required to provide the full submission for registration **within six months** of being notified of the outcome in writing; if not, the Priority determination will lapse.

This aligns with the principle that both TGA and the sponsor will commit to expediting the Priority application in the interest of public health, while also accommodating any unexpected delays in submission.



Question 6: Do you agree that there should be a six-month limit on the duration for the determination for Priority Review of biologicals?

Publication

To enhance public confidence in TGA's application of the expedited pathway, it is important that there is transparency of decisions. Transparency of decision-making will also provide useful information to sponsors who are interested in applying for the expedited pathway and help to ensure that we align with international regulators.

In line with TGA's principles for expedited pathways, it is proposed that biologicals successfully determined as eligible for the Priority Review pathway will be published on TGA's website at the time of the determination decision. Prescription medicine Priority Review applications are published [here](#). Public release of this information is made under Section 61(5A) of the [Therapeutic Goods Act 1989](#).

Transparency options for biologicals Priority Review determination decisions include:

- reporting on the total number of 'eligible' and 'ineligible' determination applications and the proportion of successful determinations in annual TGA performance reporting
- following the evaluation process, publication of the outcome and key reasons as a Decision Summary and/or Australian Public Assessment Report (AusPAR)
- for successful applications, noting in the ARTG that these biologicals went through the Priority Review pathway.



Question 7: Do you agree that we should publish the outcomes of approved applications for Priority Review determination of biologicals?

Question 8: Do you agree that Decision Summaries and/or Australian Public Assessment Reports (AusPARs) should be published for applications approved through the Priority Review pathway?

Exit criteria

In line with TGA's principles for expedited pathways, TGA will develop transparent exit criteria for instances where it may no longer be appropriate for a biological to retain its determination for Priority Review. It is proposed that the exit criteria may be triggered at any time during the registration process. When this occurs, TGA may withdraw the determination and the submission would transition to the [standard biologicals pathway](#).

Specific exit criteria will be developed in consultation with stakeholders and may differ for the Priority Review pathway. Possible exit criteria include that:

- there is evidence that at least one of the four eligibility criteria are no longer met
- the biological has been rejected for an expedited assessment process by a comparable overseas regulator and the reasons are deemed applicable within the Australian context
- the GMP requirements are no longer satisfied
- the sponsor fails to respond within a reasonable timeframe to TGA's requests for additional information.

Other considerations

Fees and charges

Our existing processes for the registration of biologicals (including application and evaluation costs) are fully cost-recovered as fees from applicants, while post-market monitoring and surveillance activities are recovered in the form of annual charges.

It is proposed there will be a new fee associated with the determination process for Priority Review pathway. This fee will apply to all applications and reflect the TGA resources required for this new determination process. Any other additional resources that are needed to implement the expedited pathway may be reflected in higher fees and charges in line with the [Australian Government Cost Recovery Guidelines](#).⁵

It is proposed to implement an application fee of approximately \$13,400 for the Priority Review determination process. This fee is based on average time required by the departmental staff in receiving, processing, reviewing and assessing the designation application against the legislative criteria and making of a decision on the application by the delegate. By way of comparison, TGA Priority Review application fees for [prescription medicines are \\$13,100](#) and for [medical devices are \\$10,300](#).

Additionally, the evaluation fees for inclusion of biologicals in the ARTG is expected to be higher under the Priority Review pathway when compared with the evaluation fees under the standard pathway. This would be necessary to recover the additional departmental costs in completing the Priority Review applications in a shorter timeframe. By way of comparison, application and evaluation fees for prescription medicines under the Priority Review pathway is approximately 5% higher than the fees payable under the standard pathway. The current TGA fees and charges can be found on the [TGA website](#).

⁵ Department of Finance 2014, Australian government cost recovery guidelines, July 2014, Third edition, Department of Finance, Canberra.

Fees will be reviewed over time to ensure they accurately represent staff effort.

Expert advice

The [Advisory Committee for Biologicals \(ACB\)](#) provides independent medical and scientific advice to the Minister for Health and TGA in relation to the safety and efficacy of biologicals. TGA has several advisory committees including ACB, [Advisory Committee on Medicines \(ACM\)](#) and [Advisory Committee on Vaccines \(ACV\)](#) that consider the supply of new therapeutic goods to the Australian market via an evidence-based evaluation of clinical data and the assessment of risk versus benefit to the Australian public.

Expert advice is also available to TGA delegates via the establishment of a specialist advisory group. The group will contain a list of specialists that have nominated to be available to provide TGA with advice as requested of them.

Flexible and timely access to external expert advice will be important to support the new priority pathway. For this reason, the pathway may use a range of options for obtaining advice, including specialist advisors and/or statutory committees. This will ensure that the expedited pathway aligns with TGA's principle that public confidence is maintained in the quality, safety and efficacy of biologicals registered via the new Priority Review pathway.



Question 9: Does the proposed application fee for a Priority Review determination and the expectation that a higher evaluation fee for an application through the Priority Review pathway seem reasonable?

Question 10: Do you anticipate utilising the Priority Review process for your products in the future?

Question 11: Please tell us any other suggestions or comments that you believe will improve the proposed Priority Review pathway for biologicals.

Appendices

Appendix 1: Expedited review pathways offered by international regulators

European Medicines Agency (EMA)

Accelerated assessment

Accelerated assessment enables EMA to reduce the timeframe for assessment of Advanced Therapy Medicinal Product (ATMP) applications for marketing authorisation from 210 days to 150 days (excluding clock stops). Applications are eligible if the Committee for Medicinal Products for Human Use (CHMP) decides that the medicine is of major interest for public health and therapeutic innovation. The CHMP may decide to continue the assessment under the standard centralised procedure assessment timelines if, at any time during the marketing authorisation application assessment, it considers that it is no longer appropriate to conduct an accelerated assessment.

Further information on accelerated assessment can be found [here](#).

US Food and Drug Administration (FDA)

The US FDA has developed expedited pathways for regenerative medicine therapies (RMT), components of which most closely align with biologicals including cell therapies, therapeutic tissue engineering products and human cell and tissue products. Expedited pathways for RMT treatment of serious or life threatening conditions include:

1. **Priority Review:** Where a Priority Review determination is granted, FDA's goal is to review an application within six months as opposed to ten months under standard review. While an applicant can expressly request priority review, the FDA decides on the review determination for every application. Eligible drugs hold the promise of delivering a significant improvement in safety or effectiveness over existing therapy for serious or life-threatening illnesses. In many instances, FDA does not take the submission to an advisory committee.
2. **Accelerated Approval:** This approval pathway allows medicines for serious conditions that fill an unmet medical need to be approved based on a surrogate endpoint or biomarker. Clinical benefit is verified through additional studies (Phase IV) conducted post-approval. Sponsors meet with FDA early in drug development to agree on the surrogate endpoint, interim analyses that may be required and relevant post-market commitments. Confirmatory trials should be underway at the time of approval, with their design and conduct agreed between the sponsor and FDA. Full approval under standard procedures may be granted after the full dataset is available.
3. **Breakthrough Therapy:** This determination is designed to expedite the development and review of drugs that treat a serious or life-threatening disease, where preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on one or more clinically significant endpoints. Medicines with the Breakthrough determination receive intensive guidance from FDA on efficient design and conduct of drug development (commencing as early as Phase I); commitment from FDA to involve senior managers and other experienced staff to facilitate efficient review; ability to obtain rolling review of data; and access to other actions to expedite review (e.g. Priority Review determination).

4. **Fast Track:** This determination is designed to facilitate the development, and expedite the review, of drugs to treat serious conditions and fulfil an unmet medical need. It involves frequent and earlier interactions between the sponsor and FDA review team through drug development (end of Phase I and II) to discuss aspects such as study design, safety data required, dose-response concerns and use of biomarkers. It also provides for rolling review of clinical data. Sponsors may apply for this determination based on nonclinical or clinical data (as opposed to clinical data only, as in the Breakthrough determination). Fast Track drugs may be eligible for Priority Review if supported by clinical data.
5. **Regenerative Medicine Advanced Therapy (RMAT) Designation:** RMAT designation includes features of the fast track and breakthrough therapy programmes, including early interactions with the FDA.

Further information on the FDA's expedited programs for RMTs is available [here](#).

Version history

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V1.0	Original publication	Biological Sciences Section, Scientific Evaluation Branch	February 2022

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