Australian Government
Department of Health
Therapeutic Goods Administration

Consultation: Guidance on variations to biologicals included in the Register

Version 1.0, September 2016

TGA Health Safety Regulation

Historical consultation document

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Chapter 1. Background

Biologicals available for general marketing in Australia have been included in the Australian Register for Therapeutic Goods (ARTG) since June 2013. The legislative basis for variations to included biologicals is in place and is equivalent to that for registered medicines. However, there is currently no guidance available to sponsors of biologicals explaining the types of changes that require submission and approval by the TGA and the business processes for varying a biological included in the Register.

This document represents draft guidance that seeks to uphold TGA's regulatory responsibilities by clarifying the intent of the existing legislation where a change is introduced to a biological included in the ARTG that:

- creates a separate and distinct good
- corrects an ARTG entry
- meets the criteria for a safety-related variation
- has the potential to impact quality, safety or efficacy.

The guidance has been presented in two chapters, '*Varying biologicals that are on the ARTG'* and *'New biologicals based on a parent biological'*. This approach has been taken to clearly highlight the different legislative basis for each application type.

Your input is sought

TGA invites comments from interested parties. Submissions may be provided on any aspect of the policies or processes outlined in the consultation document (Guidance on variations to biologicals included in the Register).

Submissions must be lodged using the online consultation submission form to upload your submission in either pdf or Word format. Alternatively, hardcopy submissions with a printed coversheet may be mailed to:

Biological Science Section

Scientific Evaluation Branch
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606

Closing date for comments is **11 November 2016**

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Chapter 2. Varying biological entries on the ARTG

This guidance is for sponsors applying for a variation to the ARTG (Australian Register of Therapeutic Goods) entry of a biological.

This guidance is:

Ü for biologicals regulated under the Biologicals Regulatory Framework that are included in the ARTG under Part 3-2A of the *Therapeutic Goods Act 1989* (the Act)

Û not for biological medicines (which are prescription medicines and registered under Part 3-2 of the Act)

For matters that **would have been relevant to the decision** to include the biological in the ARTG:

- You need to request and receive our approval for any variations or changes to or in relation to the biological.
- This is to satisfy a condition of inclusion imposed at the time of inclusion in the ARTG.

Wait for our approval

Do not implement a variation before we have approved it, otherwise you risk breaching the provisions of the *Therapeutic Goods Act 1989* (the Act):

- You are breaching a condition of inclusion in the ARTG if you implement a variation before the Secretary has approved it.
- Penalties may apply (sections 32EF (criminal offences) and 32EG (civil penalties) of the Act).

When to use this guidance

Use this guidance to determine if your change meets any of the following categories:

- creates a separate and distinct good
- corrects an ARTG entry
- has the potential to impact quality, safety or efficacy
- is a safety-related variation.

If your change does not fit within one of these categories then it is likely that, under the legislation, you are not varying your entry in the ARTG.

If you are unsure whether you need to make an application, contact the Biologicals team.

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Steps

Follow these steps to determine if your change is a variation to an ARTG entry and how to apply for approval:

1. Determine if the change would have been relevant to the inclusion decision
2. Determine if the change is a correction to your ARTG entry
3. Determine the variation category
4. Determine the supporting document requirements
5. Submit your application
6. Prepare and submit your cover letter and supporting documents
7. Pay your application fee
8. Screening of your application
9. Pay your evaluation fee
10. Evaluation of your supporting documents
11. Making a decision on your application
12. Implement the change

1. Determine if the change would have been relevant to the inclusion decision

The questions below may help identify those changes 'that would have been relevant to the decision to include the biological in the ARTG'. These questions are not exhaustive and you should not assume that they are the only indicators as to whether the change would have been relevant to the decision.

Does the change:

1. Affect compliance with a standard? Relevant standards might include:
    a. product-specific standards TGO 83-86
    b. the labelling standard (TGO 87)
    c. the donor screening and infectious disease requirements (TGO 88)
    d. pharmacopoeial monographs (default standards).
2. Alter a critical in-process control or release specification?
3. Have the potential to alter the justification used to support a critical in-process control or release specification?
    a. Justification can be by reference to limits set down in a standard, international guidance, process validation or from published literature.
    b. When information becomes available that alters the appropriateness of the justification, this could impact on the initial decision to accept the specification.

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4. Nullify or invalidate previous validation studies?

    a. A manufacturing process or method needs to be supported by current validation studies submitted and accepted by TGA.

    b. Re-validation should occur and data be submitted if the changed process or method is not supported by current studies.

5. Alter a manufacturing process or test method, including changes to infectious disease test kits?

6. Alter a critical material that affects the critical quality and safety parameters?

    a. defined as supplies or reagents that come in direct contact with the cell or tissue during any stage of manufacture, such as primary containers or collection kits.

    b. includes containers and materials of human and animal origin

    c. critical parameters are those that determine suitability for the intended purpose e.g. quality control specifications, sterility and biocompatibility

7. Introduce a new manufacturing site or change the scope of activities performed at a current manufacturing site?

8. Involve generation of a new Master Cell Bank or Working Cell Bank?

9. Alter the formulation or composition of the finished product?

10. Alter the approved risk-benefit profile?

11. Alter the intended clinical use or therapeutic indication?

12. Alter the intended clinical use/therapeutic indication (including safety-related changes)?

If the answer to any of these questions is 'yes', it is likely that the variation will have the potential to affect the quality, safety or efficacy of the product and require submission to TGA and approval prior to implementation. For changes that require submission to TGA go to Step 3 of this guidance to determine the category of the change and if it requires evaluation or is 'self-assessable'.

If the answer to all of these questions is 'no', then it is possible that an application to vary your ARTG entry is not required. The exception is if the change could be considered a correction to your ARTG entry (Step 2, below).

2. Determine if the change is a correction to your ARTG entry

If you want to correct an ARTG entry that is incomplete or incorrect, apply to the TGA under subsection 9D(1) of the Act.

Corrections

Apply for a correction when:

· There are spelling or grammatical errors in the ARTG entry

· Information is incorrect or absent from the ARTG entry

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- A correction needs to be made to information previously submitted in support of the inclusion of the biological. This is limited to changes that do not require evaluation of new information, e.g. correction to a policy, standard operating procedure or validation report
- There are typographical errors in the product information or labels that need to be changed to align with the ARTG entry details.

Changes that are not corrections

The change will not be considered a correction to the ARTG details under subsection 9D(1) if the matter could have been relevant to the decision to include your biological in the ARTG or any later decision to vary the ARTG entry.

For example, a change is not a correction where evaluation of incorrect or incomplete information is required, because it has the potential to impact on the initial decision to include the biological in the ARTG.

When you are correcting an ARTG entry

There is no fee to correct an ARTG entry for a biological. To complete your online application, you need a fee exemption code:

1. Draft an application (Step 5. Start your application).
2. Contact the Biologicals team by email requesting a 'fee exemption code' for an application under subsection 9D(1) to correct an ARTG entry, making reference to the draft application number.
3. Once a fee exemption code has been generated, the application form can be submitted
4. Prepare a cover letter to support the change (Step 6. Prepare your cover letter).
5. Submit your application (Step 7).

If your change would not have been relevant to the initial decision (Step 1), and is not a correction to your ARTG entry (Step 2), then it is likely that no application to vary your entry in the ARTG is required.

If your change is relevant to the initial decision, you will need to determine what category it fits into.

3. Determine the variation category

Determine the variation category:

a. Determine if the change creates a separate and distinct good

b. Determine if the change is safety-related

c. Other changes with the potential to impact quality, safety and efficacy

a. Determine if the change creates a separate and distinct good

If you are making a change that creates a separate and distinct good (see regulation 11A, Therapeutic Goods Regulations 1990), you are not varying the entry for an existing biological, but creating a new one.

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Class 1 and 2 biologicals

For Class 1 and 2 biologicals, changing any of the following will create a separate and distinct good:

- applicable standards (e.g. TGO 83-88, default pharmacopeial standards)
- intended clinical use
- principal manufacturer

Class 3 and 4 biologicals

For Class 3 and 4 biologicals, changing any of the following will create a separate and distinct good:

- product name
- dosage form
- formulation or composition
- therapeutic indication
- type of container, regardless of container size
- principal manufacturer.

New biologicals based on parent (already approved) biologicals

If you are creating a separate and distinct good:

ü Apply for a new biological based on a parent biological

û Do not apply for a variation.

b. Determine if the change is safety-related

Safety-related variations made under section 9D(3AA) of the Act are limited to variations that:

- reduce the patient population
  - for example, limiting the use of the biological
- add a warning or precaution
  - for example, about an adverse event or interaction

If the therapeutic indication changes as a result of a safety-related variation, it will not be treated as a separate and distinct good.

If you **change the therapeutic indication** of a class 3 or 4 biological, but **NOT** as a result of a safety-related variation, you are creating a separate and distinct good:

ü Apply for a new biological based on a parent biological

û Do not apply for a variation under section 9D(3AA).

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Justify

Explain how your variation meets the criteria for a safety-related variation.

Safety-related variations always require changes to the release documentation outlining warning statements e.g. Product Information sheet. Where appropriate to support the changes, submit additional supporting documents.

If the proposed change is more than adding a simple word or phrase to release documentation, or is intended to reflect new quantitative findings from a clinical trial or other type of study, the TGA is likely to need to evaluate supporting data.

However, it is possible that safety-related changes can be considered 'self-assessable' and do not require evaluation of the supporting data. These may be identified on TGA screening of the application. The evaluation fee does not apply to self-assessable variations.

Examples of safety-related requests for prescription medicines, including those that may not require evaluation of the supporting data are available.

Assessing your justification

We will grant your request if we agree that your variation:

- meets the criteria for a safety-related variation
- does not create a separate and distinct good.

We may need to evaluate the supporting documents to make this decision.

Sometimes we contact you

We contact you when we become aware of safety-related information that requires a safety-related variation to one of your ARTG entries. This might be because:

- we have identified a signal during post-market monitoring
- other ARTG entries of a similar kind have been varied for safety-related reasons.

In this instance a response will be sought from you, which may result in the need to submit a safety-related variation.

Changes that are not safety-related

If your variation is not considered to be safety-related, it may still have the potential to impact quality, safety or efficacy.

c. Other changes with the potential to impact quality, safety and efficacy

This section refers to changes that have the potential to affect the quality, safety or efficacy of the biological (under section 9D (3A)), provided that the change does not create a separate and distinct good.

Based on the level of review required, variations under 9D (3A) are split into 3 categories:

- self-assessable variations
- minor variations
- major variations

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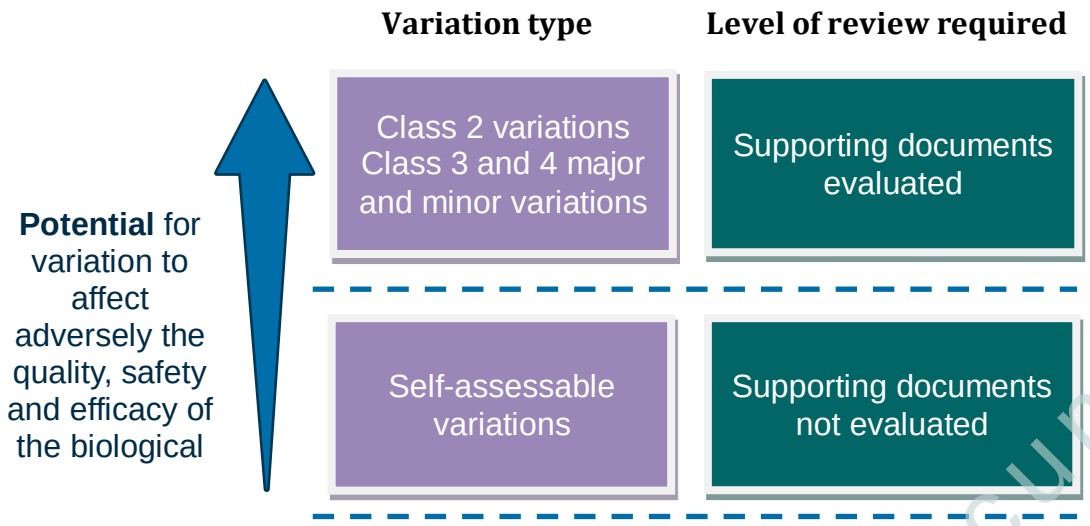

The definitions for the main categories of variations are provided below:

Application Category	Definition
Self-assessable variations	Applies to variations that do not require evaluation of information and would be expected to have minimal effect on the quality, safety or efficacy of the biological.
Minor variation	Applies to a variation that requires the evaluation of quality and manufacturing information, other than a change that is a major variation for the biological or that would result in the biological becoming separate and distinct from other biologicals.
Major variation	Applies to a change to the entry for any of the following: a. a change requiring submission and evaluation of clinical data b. a new strength c. a new route of administration d. a change in the intended patient group e. a change in dosage.

The following provides guidance on the types of changes that do not require evaluation of the supporting documents (self-assessable variations).

By default, if the change does not meet the definition of a self-assessable variation then the change will be treated as a minor or major variation, as defined above.

Self-assessable variations

For some variations with the potential to impact the quality, safety and efficacy of the biological (including some safety-related variations), the supporting documents may not require evaluation.

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Applications that do not require evaluation of the supporting documents are termed '**self-assessable' variations**.

To determine if your variation is self-assessable:

- check the defined self-assessable variations, or
- conduct a risk assessment.

Defined self-assessable variations

Your supporting documents do not require evaluation (i.e. are self-assessable) if:

- your variation is one of the defined self-assessable variations; and
- all conditions that are relevant to that variation are met.

As experience with variations to ARTG entries for biologicals increases, we anticipate adding to the list of defined self-assessable variations.

Table of defined self-assessable variations

Change	Conditions
Infectious disease test kit change	a. No decrease in specificity, sensitivity, limit of detection and accuracy b. Performed as per kit instructions, including the intended use c. Same level of regulatory approval of the kit d. TGA GMP certification of the testing facility
Reduction in shelf-life of product or shipping timeframes	a. Revised specifications are still within the scope of the TGA approved validation studies b. No quality or safety concerns triggered the change
New manufacturing site	a. No changes to the approved manufacturing processes b. TGA GMP certification of the manufacturing site for that step c. No need to perform validation of the manufacturing process at the site d. The new manufacturing site is not responsible for donor screening and testing
Donor selection criteria, including the medical and social history questionnaire	a. More stringent donor selection criteria (previously acceptable donors would now be rejected) b. In compliance with TGO 88

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Change	Conditions
Critical material change	a. The critical parameters are equivalent or of greater quality[1] b. The material is not an excipient c. The material is not of human or animal origin
In-process or release specifications change	a. More stringent specifications b. Still in compliance with any applicable standard
Previously approved variation to another biological	a. Sponsor must be the same for current and previous applications b. Variation must have the same potential effect upon the two biologicals c. Relevant regulatory requirements must not have changed since the approval date of previous variation

[1] Note that changes to some critical materials may have a more significant impact on the product than others and may require evaluation of the supporting data. For example, a change to the quality of a growth supplement (critical material) can have a significant effect on the culture conditions and would often require re-validation of the manufacturing process; A change to a primary container (critical material) may require re-validation of product stability.

Conducting a risk assessment

If your change is not listed in the *Table of defined self-assessable variations*, then you will need to conduct a risk assessment to determine the potential of the change to adversely affect the quality, safety or efficacy of the biological. You will need to submit this risk assessment with your variation request.

The variation must have only a low potential to adversely affect the quality of the biological in order to not require evaluation of the data by the TGA.

Note that if a subsequent review of the change identifies a greater potential to impact the quality safety or efficacy of the biological then it may require evaluation of the supporting data.

Contact us

If you are unsure on the variation category or whether your supporting documents require evaluation, contact the Biologicals team.

4. Determine the supporting document requirements

Most variations require documents to be provided to support an application. Corrections to ARTG entries under subsection 9D(1) of the Act may not require any supporting documentation.

The level of supporting documentation required for variations depends on:

- the complexity of the change
- the potential to adversely affect the quality, safety and efficacy of the good.

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The following supporting information and documents should be provided, where applicable:

- details as to how the variation changes information held by TGA in regard to a biological on the ARTG
- documents to support the variation e.g. validation data, operating procedures, literature references, updated specifications

Supporting documents may include copies of:

- amended procedural documentation and specifications (including a marked up and a clean copy to allow side-by-side comparison)
- amended labels and product information sheets
- new test methods
- method or process validation studies
- published literature used to support a change
- safety and efficacy study reports (complete reports)
- any other relevant information.

The guidance provided in Step 3 (Determine the variation category) will determine whether the supporting documents require evaluation or not.

5. Submit your application

To make your application:

- Know your ARTG number
- Decide how many applications to make
- Fill out the form

Know your ARTG number

You need to know the ARTG number for the biological. Once you enter this number in the form, the data in the current ARTG entry will be placed into the form:

- you will be able to change information in most of the fields
- some fields are locked, because they cannot be changed in a variation application.

Decide how many applications to make

Consider the following:

- multiple variations in a single application
- multiple products
- multiple ARTG entries

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Multiple variations in a single application

You can combine multiple variations to a biological or biologicals in a single ARTG entry within one application (except for safety-related changes), where they fit more than one category of variation.

The following categories of variations can (tick) and cannot (cross) be combined in a single application:

ü correcting an entry, self-assessable and minor variations

û major variation or safety-related changes

Consider the following aspects carefully when deciding whether to submit a single application with multiple variations or make a separate application for each variation:

- Where a single application contains multiple variations in relation to biological in a single ARTG entry, the TGA will consider the acceptability of each of the variations individually.
- Self-assessable variations submitted in a single application with one or more variations that require evaluation cannot be approved and implemented until a decision is made for all variations in the application.
- As the TGA considers each variation on its merits, the non-approval of any of the variations within an application containing multiple changes would not result in rejection of the entire application.
- Where the TGA identifies questions with any of the variations, the decision on the application will be delayed until all issues have been resolved.

Multiple products

For Class 2 biologicals, you can apply to vary some or all products contained within a single ARTG entry. This does not apply to class 3 and 4 biologicals as there is only a single product included under each ARTG entry.

Multiple ARTG entries

One application must be made for each ARTG entry.

Where you are introducing the same variation to separate entries on the ARTG, an application is required for each ARTG entry, but the TGA may review them simultaneously for evaluation purposes.

If the following criteria are met then you should submit your multiple applications as a single **simultaneous submission**:

- same sponsor
- same active ingredient (active biological component)
- same standards apply
- same principal manufacturer

Guidance on how to submit the multiple applications as a single submission are provided in the Australian Regulatory Guidance for Biologicals (ARGB) Appendix 10.

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If the applications do not meet these criteria then you cannot make a simultaneous submission, but the applications (if from the same sponsor) may still be treated as abridged applications if:

- the same change is being applied for in the two applications and the change will affect the two biologicals in the same way
- your cover letters for the applications refer to each other and you request that the applications be considered together
- you explain how the applications are similar.

Reduction or waiver of the evaluation fees may apply to simultaneous submissions and abridged applications.

Fill out the form

For all variations to a biological included in the ARTG, you must submit an application via TGA Business Services. See the ARGB, Appendix 10 for detailed instructions.

6. Prepare and submit your cover letter and supporting documents

This step applies to requests for all variations.

Prepare a cover letter for a:

- correction
- safety-related
- other variations (self-assessable)
- other variations (not self-assessable)
- variations that impact multiple applications

Corrections cover letter

In your cover letter for a correction to an ARTG entry, include:

- the variation category and section of the Act that you are making your application under:
  - 'This application is to correct an ARTG entry of a biological and is made under subsection 9D(1) of the *Therapeutic Goods Act 1989*'
- reference to the application number (following submission of the online application form; Step 4)
- an explanation of why this variation is simply a correction i.e. what information is incomplete or incorrect and how
- details clearly highlighting the proposed change/s, such as a marked up copy of a document.

If you refer to previously submitted documents, provide sufficient details for us to be able to locate the documents easily.

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Safety-related cover letter

In your cover letter for a safety-related variation, include:

- the variation category and section of the Act that you are making your application under:
  - 'This application is a safety-related variation for a biological and is made under subsection 9D(3AA) of the *Therapeutic Goods Act 1989*'
- reference to the application number
- an explanation of how the proposed change meets the criteria for a safety-related variation
- details clearly highlighting the variations, such as a marked up copy of a document
- if you are including supporting documents provide a list of these.

Other variations (self-assessable) cover letter

In your cover letter for a self-assessable variation, include:

- the variation category and section of the Act that you are making your application under:
  - 'This application is a self-assessable variation for a variation to a biological with potential to impact the quality, safety and efficacy (but not resulting in the reduction of quality, safety or efficacy) and is made under subsection 9D(3A) [or subsection 9D(3AA) for safety-related changes] of the *Therapeutic Goods Act 1989*'
- reference to the application number
- details of the variations
- a justification for why you think the variation is self-assessable, with sufficient detail for us to be able to determine quickly whether it is appropriately classified.
- a declaration that your changes meet the conditions that apply to defined self-assessable variations, if applicable.
- if the variation is not a defined self-assessable variation, an explanation of how your risk assessment supports a low-risk classification.
- the proposed timing and approach to implementing the variation, including the expected time period during which the pre-variation and post-variation products might be supplied concurrently.
- a list of the supporting documents being provided.

If you refer to previously submitted documents, provide sufficient details for us to be able to locate the documents easily.

If third party documents are provided directly to TGA to support the change, you also need to provide a letter of access from the relevant third party stating that you have the authority to rely on them as supporting information.

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Other variations (not self-assessable) cover letter

In your cover letter for a variation with potential to impact the quality, safety and efficacy (but not so as to reduce the safety, quality or efficacy) when evaluation of supporting documents is required, include:

- the variation category and section of the Act that you are making your application under:
  - 'This application is for a [variation/minor variation/major variation] to a class [2/3/4] biological with potential to impact the quality, safety and efficacy and is made under subsection 9D(3A) of the *Therapeutic Goods Act 1989*'
- reference to the application number
- details of the variations, and a justification as to why the quality, safety & efficacy has not been reduced.
- the proposed timing and approach to implementing the changes, including the expected time period during which the pre-variation and post-variation products might be supplied concurrently.
- a list of the supporting documents provided.

If you refer to previously submitted documents, provide sufficient details for us to be able to locate the documents easily.

If third party documents are provided directly to TGA to support the change, you also need to provide a letter of access from the relevant third party stating that you have the authority to rely on them as supporting information.

Variations that affect multiple products

If you are making similar applications to vary biologicals in multiple ARTG entries (e.g. simultaneous and abridged applications):

- include the application numbers from TGA Business Services of the other applications.
- explain how the applications are similar, and indicate whether a reduction or waiver of the evaluation fee is being sought.

7. Pay your application fee

There is no application or evaluation fee for making corrections to an ARTG entry for a biological under subsection 9D(1). The use of the fee exemption code in the application form prevents invoicing for the application fee.

For all other applications, you need to pay the application fee at the time the application is submitted. Following submission, the acknowledgement of successful submission invites you to print a copy of your invoice.

For information on payment methods go to:

- Payment options

We will not consider your application until you have paid your application fee.

For details of the current fees, go to:

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- Schedule of fees and charges

8. Screening of your application

Once we receive your application, application fee and supporting data (if applicable), we review your application and decide:

- if the appropriate variation category has been applied
- whether the supporting documents require evaluation
- the appropriate evaluation fee.

Letter

At the completion of the screening we will send you a letter informing you of:

- the variation category
- the decision, for:
  - corrections to ARTG entries [9D(1) applications]
  - self-assessable variations, when unaccompanied by other variations (Go to Step 12.)
- for all other applications:
  - whether we accept the application for evaluation (sufficient supporting documents are provided)
  - the evaluation fee (invoicing will follow receipt of the letter)
  - the anticipated TGA timeframe for evaluation and decision.

Screening timeframe

We aim to accomplish the screening of most applications in 15 working days.

Our legislated timeframe is 30 days for notification of whether we will evaluate the application (regulation 16GB, Therapeutic Goods Regulations 1990)

No timeframe is set for corrections to ARTG entries [applications under section 9D(1)].

Evaluation fees

An additional fee applies to the application if the supporting documents require evaluation.

The fee depends on the variation category:

- safety-related
- potential to impact quality, safety and efficacy
  - variation to class 2 biological
  - minor variation
  - major variation

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Standard evaluation fees are defined in the Schedule of fees and charges.

However, we are also able to reduce or waive the evaluation fee, so that it corresponds to the level of supporting documents and assessment required [regulations 45(2) & 45(4) of the Therapeutic Goods Regulations 1990]. We might reduce the fee:

- if you make another application(s) in relation to therapeutic goods at the same time and the following circumstances apply (simultaneous submission):
  - the goods to which each application relates contain the same active ingredient
  - the information given in support of each application has sufficient commonality, in respect of the goods, that a simultaneous evaluation of the goods may conveniently be made
- if the Secretary has information relating to the goods that enables the evaluation procedure to be abridged (abridged application).

9. Pay your evaluation fee

Following screening of your application, if evaluation of the supporting information is required you will be sent an invoice for an evaluation fee.

There is no evaluation fee for:

- making changes corrections to the ARTG entry under section 9D(1)
- self-assessable variations.

For details of the current fees, go to:

- Schedule of fees and charges

For information on payment methods go to:

- Payment options

10. Evaluation of your supporting documents

We will evaluate most applications within the TGA target timeframes below. The letter we send you at the end of the screening will state the anticipated TGA timeframe for evaluating your application.

Screening and evaluation timeframes for variations to biologicals

Application category	TGA target timeframes (screening + evaluation)
Correction to an ARTG entry	15 working days in total
Self-assessable variation	15 working days
Safety-related changes	TGA processes as soon as possible

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Application category	TGA target timeframes (screening + evaluation)
Variations of class 2 biologicals	15 + 45 working days
Minor variation	15 + 45 working days
Major variation	15 + 255 working days

When you have applied for multiple variations that fit more than one category, the applicable timeframes will reflect the highest level of category change. For example, if you have applied for a number of self-assessable variations and one minor variation, the timeframes will be those of the minor variation.

The legislated evaluation time for variation applications under sections 9D(3A) and 9D(3AA) is 255 working days (regulation 16GD, Therapeutic Goods Regulations 1990). There are some exceptions to the target internal timeframes, for example:

- priority will be given to safety-related changes
- when an application with a target timeframe of 45 days is complex, we will take longer than 45 working days for the evaluation and decision
- you will be advised of a longer timeframe for evaluation of your application in the letter send to you following screening.

Requests for information

We may ask you for more information under section 32JA of the *Therapeutic Goods Act 1989*.

It is an offence not to comply with such a notice or to provide information that is false or misleading in a material particular.

We must allow you at least 14 days from when you receive the notice, to provide the information and documents. The response period will be clearly stipulated in the section 32JA letter. If we have not given you sufficient time to respond, you may ask us for an extension in writing by contacting the Biologicals team.

The period of time from when we send a request under section 32JA to when you respond, does not count towards TGA working days.

11. Making a decision on your application

Once we have made our decision, we will send you a decision letter. We make our decisions on all the applications within a simultaneous submission at the same time.

Read the decision letter carefully, especially the list of changes approved and the timeframe for implementation. If you have applied for more than one variation in an application, it is possible that we may approve some of the variations and not others.

Approval with conditions on the inclusion

As part of the approval the Secretary may consider whether additional conditions need to be imposed under section 32EE of the Act.

Historical consultation document

Rejection

If the decision is to reject some or all of the variations in your application, the decision letter will include both:

- a statement of the reasons for the decision
- information on your rights to seek a review of the decision.

12. Implement the change

Wait for approval before implementing a change. You are breaching a condition of inclusion in the ARTG if you implement a variation before the Secretary has approved it.

If a variation results in improved quality or safety, we may also impose a new condition of inclusion under section 32EE with a timeframe for implementing the change.

On rare occasions, some changes beyond your control may take place before the TGA can approve them (for example, a change to a test kit used by a contracted facility). In these cases, it is your responsibility to submit a request to the TGA as soon as you become aware of the change.

Historical consultation document

Chapter 3. New biologicals based on a parent biological

This guidance is for sponsors of biologicals included in the ARTG who want to make a change to that biological (parent biological) where the change creates a separate and distinct good (new biological).

Determine if you are creating a separate and distinct good is Step 3 of the process to vary a biological. There are separate definitions of 'separate and distinct good' for the lower risk classes (class 1 and 2) and the higher risk classes (class 3 and 4) in regulation 11A of the Therapeutic Goods Regulations 1990.

This guidance does not apply to biological medicines, which are prescription medicines.

On this page: Preparing your explanation; How we reduce your fees; Application process; Cancelling parent biological

Preparing your explanation

Prepare a sufficiently detailed explanation of how the new biological is based on the parent biological.

We will use this explanation to determine:

- the extent to which the evaluation procedure can be abridged
- how much to reduce the evaluation fee.

If you want to maintain two entries on the ARTG (the new biological and the parent biological) the new entry must have a different name from the parent entry.

How we reduce your fees

If we have information relating to the goods that enables the evaluation procedure to be abridged, we can reduce the evaluation fee (regulation 45(4) of the Therapeutic Goods Regulations 1990). The evaluation fee can be adjusted to reflect the level of supporting information and assessment required.

We will:

- consider your explanation detailing how the new biological is based on a parent biological
- consider the level of supporting data provided to support the application
- make a determination about fee reduction on a case-by-case basis.

Historical consultation document

Application process

To apply for a new biological under section 32DD of the *Therapeutic Goods Act 1989* refer to guidance provided in the Australian Guidelines for Biologicals.

The level of supporting information required depends on:

- the degree of the change from the parent biological
- the potential of the change to impact on the quality, safety and efficacy of the good.

Cancelling parent biological

If we approve your application for a new biological based on a parent biological, you may either:

- maintain both entries (provided the entries have different names)
- cancel the parent biological from the ARTG.

Instructions on how to request to cancel an ARTG entry can be found on our website. Requests can be made through the TGA Business Services portal or by completion and submission of a paper form.

Version history

Version	Description of change	Author	Effective date
V1.0	Published for consultation	Biological Sciences Section Regulatory Guidance Team	September 2016

Historical consultation document

Historical consultation document

Therapeutic Goods Administration

PO Box 100 Woden ACT 2606 Australia
Email: info@tga.gov.au Phone: 1800 020 653 Fax: 02 6232 1605
https://www.tga.gov.au