Minor variations to prescription medicines

Appendix 2: Variation change types – biological medicines

Version 2.1, January 2018
Minor variations to biological prescription medicines: Appendix 2: Variation change types – biological medicines
V2.1 January 2018
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Introduction

The Therapeutic Goods Administration (TGA) takes a risk-based approach to assessing variations to prescription medicines. This means that the higher the risk associated with the variation, the greater the level of assessment required by the TGA for a decision to be made.

This guidance outlines the following types of minor variations and changes that can be made to biological medicines currently on the Australian Register of Therapeutic Goods (ARTG):

- Changes that do not require prior approval. These are:
  - changes that can be implemented without informing the TGA and
  - changes that can be implemented before you inform the TGA of the change.

- Corrections to an ARTG entry – a minor change to correct or complete information that was inadvertently recorded incorrectly or omitted in the ARTG entry, including the product information (PI).

- Notifications – very low risk variations with specific conditions. TGA approval for these variations is made automatically upon lodgement and payment of the application. The applicant must provide legal assurances that all conditions are met and submit supporting data using the approved electronic form.

- Minor Editorial Changes to product information (MEC).

- Self-Assessable Requests (SARs) – lower risk variations for which the sponsor can provide an assessment of their own data for the TGA to verify.

- Safety Related Requests (SRRs) – requests to either reduce the patient population that can receive the medicine or add a warning or precaution.

- Category 3 requests – variations that require evaluation of quality-related data only. The change types listed in this guidance are representative and are not intended to be an exhaustive list of all quality-related changes requiring evaluation of data.

Major variations (Category 1 applications) are not covered by this guidance. These require evaluation of a full dataset, or any combination of quality, nonclinical, clinical and bioequivalence data. See the Prescription medicines registration process for information on how to lodge a Category 1 application.

Data supporting minor variations requests

The conditions outlined within each variation type set out the minimum documentation required for regulatory purposes, but depending on the particular circumstances surrounding the change, additional data may be needed. Additional data may also need to be generated to meet requirements under Good Manufacturing Practice.

Refer to each type of change for full data requirements.
## Index of change codes — biological medicines

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**Site of manufacture changes**

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| Report separately | Manufacturing — changes to the acceptance criteria for raw materials        | Requires reporting to the TGA but not prior approval |
| Report separately | Manufacturing — changes to manufacturing process documentation (editorial)  | Requires reporting to the TGA but not prior approval |
| OAMS       | Albumin — change of manufacturer's name or contact details                   | Notification      |
| PMRS       | Drug product site of manufacture — addition of new site of release-for-supply operations for a registered drug product | Notification      |
| OHMS       | Heparin (crude) — change of heparin manufacturer or supplier                | SAR               |
| PDDM       | Drug product/substance site of manufacture — cessation of a site or deletion of a manufacturing step | SAR               |
| PDQC       | Drug product/substance site of manufacture — change to quality control testing site | SAR               |
| PMER       | Drug product site of manufacture — change to manufacturer or supplier of excipients or raw materials | SAR               |</p>
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**In-house reference standard changes**

- **IRSR**: In-house reference standard — replacement
- **IRNA**: In-house reference standard — changes

**Purification process changes**

- **PPCR**: Purification process — column life reduction
- **PPHR**: Purification process — holding time reduction for a non-plasma-derived product

**Filling changes**

- **FLIS**: Filling — introduction of a similar filling line
- **PFNP**: Filling — changes to drug product filling

**Changes to storage of drug substance**

- **ASRS**: API storage conditions — reduction in shelf life
- **ACMR**: API storage conditions — change of storage container dimensions or manufacturer

**Changes to storage of drug product**

- **CASL**: Shelf life / storage condition
- **PSLD**: Drug product storage conditions — reduction in shelf life
- **PSET**: Drug product storage conditions — changes to excursion temperature during manufacture
- **PSAR**: Drug product storage conditions — addition of a restrictive shelf life or storage condition
- **PSLC**: Shelf life — changes to shelf life or storage conditions of a drug product

**Fermentation process changes**
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**Plasma Master File changes**

- Report separately
- Plasma — master file changes
  - Requires reporting to the TGA but not prior approval
- PMFC
  - Plasma — master file changes
  - Category 3

**Plasma fractionation intermediates changes**

- PFCR
  - Plasma — changes to fractionation intermediates — column life reduction
  - Notification
- PFSC
  - Plasma — changes to fractionation intermediates — more stringent internal process control
  - Notification
- PFIC
  - Plasma — changes to fractionation intermediates
  - Category 3

**Product information (PI) changes**

- CAPI
  - Product Information (PI)
  - Correction
- PIME
  - PI — Make minor editorial changes
  - MEC
- PIAE
  - PI — adding the names of excipients in the product
  - SAR
- PICA
  - PI — adding the Chemical Abstracts Service (CAS) number, molecular formula/weight and/or chemical structure/nomenclature of the API
  - SAR
- PIPD
  - PI — changing the PI of radiopharmaceuticals to give instructions that the patient dose should be measured immediately before administration
  - SAR
- PIPS
  - PI — changing the name, address or other details of the product’s sponsor or distributor
  - SAR
- PIRI
  - PI — changing the PI of radiopharmaceuticals to give instructions/information on radiation protection and safety of user and patient
  - SAR
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### Product label changes

Changes to labels that do not require reporting to the TGA. This includes:

- change to AUST R number following an approved change that requires a new AUST R number
- inclusion or removal of, or changes to, sponsor or supplier telephone/facsimile number, email address, barcodes, ABN or Australian Company Number, product code number, patent number, recycle logo and associated text, trademark and other such symbols
- changes to colours of artwork
- inclusion or removal of date of manufacture of product
- inclusion or removal of foreign national registration number
- inclusion or removal of, or changes to, name and address of supplier in New Zealand
- change of typeface and increase in font size of print only
- change in web address, without a change in the content of the website.

Does not require reporting to the TGA

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Variation category</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPCL</td>
<td>Label — addition or deletion of, or change to, the company logo or livery</td>
<td>Notification</td>
</tr>
<tr>
<td>LPCP</td>
<td>Label — addition or deletion of, or change to, the pictogram of a product or its dosage form</td>
<td>Notification</td>
</tr>
<tr>
<td>LPCS</td>
<td>Label — addition or deletion of, or change to, the name or address of the Australian sponsor or supplier of the product</td>
<td>Notification</td>
</tr>
<tr>
<td>LPDG</td>
<td>Label — deletion of existing graphics, pictures or diagrams, and any associated text</td>
<td>Notification</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
<td>Variation category</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>LPDR</td>
<td>Label — deletion of repeated text (present elsewhere on a label) from selected side panels provided that the information is not mandatory</td>
<td>Notification</td>
</tr>
<tr>
<td>LPIA</td>
<td>Label — addition/deletion of, or change to, simple instructional, informational or anti-tampering statements as outlined in the TGA Guidance</td>
<td>Notification</td>
</tr>
<tr>
<td>LPOP</td>
<td>Label — addition/deletion of, or change to text of outer protective pouches or overwraps as outlined in the TGA guidance</td>
<td>Notification</td>
</tr>
<tr>
<td>LOAI</td>
<td>Label — addition of a new TGA-approved route of administration for injectable medicines</td>
<td>SAR</td>
</tr>
<tr>
<td>LOCA</td>
<td>Label — changes as a result of approved corrections made to an entry in the ARTG.</td>
<td>SAR</td>
</tr>
<tr>
<td>LOCN</td>
<td>Label — changes to names of actives, excipients or dosage forms resulting from changes in the AAN, ingredients database or code tables in TGA eBS.</td>
<td>SAR</td>
</tr>
<tr>
<td>LOEI</td>
<td>Label — changes to the method of expressing the content of active ingredients or excipients, in accordance with the current labelling TGO.</td>
<td>SAR</td>
</tr>
<tr>
<td>LOPR</td>
<td>Label — changes as a result of product rescheduling (following from changes to the Poisons Standard).</td>
<td>SAR</td>
</tr>
<tr>
<td>LOPS</td>
<td>Label — amendments due to implementation of changes that do not require prior notification to the TGA.</td>
<td>SAR</td>
</tr>
<tr>
<td>LOSA</td>
<td>Label — amendments resulting from the implementation of a SAR that is either submitted simultaneously or has been previously approved by the TGA.</td>
<td>SAR</td>
</tr>
<tr>
<td>LOTG</td>
<td>Label — changes to comply with current TGOs for labels that have previously been evaluated and approved by the TGA.</td>
<td>SAR</td>
</tr>
<tr>
<td>LPCO</td>
<td>Label — addition/deletion of, or change to, the statement of country of origin or manufacture for imported products.</td>
<td>SAR</td>
</tr>
<tr>
<td>LPDL</td>
<td>Label — changes to the colour, design or layout of labels with no change to content and retaining differentiation of strengths.</td>
<td>SAR</td>
</tr>
<tr>
<td>LPSP</td>
<td>Label — change to the layout or design of a physician sample pack.</td>
<td>SAR</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
<td>Variation category</td>
</tr>
<tr>
<td>---------</td>
<td>------------------------------------------------------------------------------</td>
<td>--------------------</td>
</tr>
<tr>
<td>LPWS</td>
<td>Label — addition or deletion of, or change to, the website address of an Australian owned and managed company.</td>
<td>SAR</td>
</tr>
<tr>
<td>LQAB</td>
<td>Label — addition of excipients</td>
<td>SAR</td>
</tr>
<tr>
<td>LQBM</td>
<td>Label — amendment of expression of API content in topical preparations as previously approved.</td>
<td>SAR</td>
</tr>
<tr>
<td>LQHB</td>
<td>Label — addition of 'hypotonic', 'hypertonic' and 'isotonic' for large-volume injections.</td>
<td>SAR</td>
</tr>
<tr>
<td>LQRB</td>
<td>Label — addition of a previously approved release rate for transdermal patches.</td>
<td>SAR</td>
</tr>
<tr>
<td>LWAB</td>
<td>Label — addition of a warning or cautionary statement where an incorrect route for method of administration is hazardous</td>
<td>SAR</td>
</tr>
<tr>
<td>LWSB</td>
<td>Label — changes to/addition of a warning or precaution statement resulting from an approved safety-related variation to the PI.</td>
<td>SAR</td>
</tr>
<tr>
<td>LCDE</td>
<td>Label changes — any changes requiring data for evaluation</td>
<td>Category 3</td>
</tr>
<tr>
<td>DTTR</td>
<td>Trade name replacement</td>
<td>Category 3 - separate &amp; distinct good</td>
</tr>
</tbody>
</table>

**Pack size changes**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Variation category</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPS</td>
<td>Pack size &amp; poison schedule</td>
<td>Correction</td>
</tr>
<tr>
<td>PPRU</td>
<td>Pack size — reduction of number of units in pack size excluding volume of fill of injections or other sterile preparations</td>
<td>SAR</td>
</tr>
<tr>
<td>PSCA</td>
<td>Packaging — change to or addition of pack size</td>
<td>Category 3</td>
</tr>
</tbody>
</table>

**Drug product packaging changes**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Variation category</th>
</tr>
</thead>
<tbody>
<tr>
<td>CACI</td>
<td>Correct an ARTG entry — Container information</td>
<td>Correction</td>
</tr>
<tr>
<td>PPAT</td>
<td>Packaging — introduction of anti-tamper packaging (materials not in contact with drug product).</td>
<td>Notification</td>
</tr>
<tr>
<td>CCPC</td>
<td>Packaging — changes</td>
<td>Category 3</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
<td>Variation category</td>
</tr>
<tr>
<td>-------</td>
<td>-------------------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------</td>
</tr>
<tr>
<td>PCCT</td>
<td>Packaging — Changes to container type</td>
<td>Category 3 - separate &amp; distinct good</td>
</tr>
<tr>
<td></td>
<td><strong>Changes specific to influenza vaccines</strong></td>
<td></td>
</tr>
<tr>
<td>IVMP</td>
<td>Influenza vaccine — strain-specific variations to manufacturing processes.</td>
<td>SAR</td>
</tr>
<tr>
<td>IVPL</td>
<td>Influenza vaccine — passage or lot number change of approved reassorted virus or approved virus isolate.</td>
<td>SAR</td>
</tr>
<tr>
<td>IVRR</td>
<td>Influenza vaccine — reference reagent replacement</td>
<td>SAR</td>
</tr>
<tr>
<td>IVSL</td>
<td>Influenza vaccine — working seed lot change</td>
<td>SAR</td>
</tr>
<tr>
<td>IVSC</td>
<td>Influenza vaccine changes</td>
<td>Category 3</td>
</tr>
<tr>
<td></td>
<td><strong>Other changes</strong></td>
<td></td>
</tr>
<tr>
<td>CADF</td>
<td>Correct an ARTG entry — Dosage form</td>
<td>Correction</td>
</tr>
<tr>
<td>CAIC</td>
<td>Correct an ARTG entry — Indications</td>
<td>Correction</td>
</tr>
<tr>
<td>CANC</td>
<td>Correct an ARTG entry — ATC Nordic codes</td>
<td>Correction</td>
</tr>
<tr>
<td>CAQI</td>
<td>Correct an ARTG entry — Quality-related information, includes labels.</td>
<td>Correction</td>
</tr>
<tr>
<td>CARA</td>
<td>Correct an ARTG entry — Route of administration</td>
<td>Correction</td>
</tr>
<tr>
<td>CASI</td>
<td>Correct an ARTG entry — Sterility information</td>
<td>Correction</td>
</tr>
<tr>
<td>CAVI</td>
<td>Correct an ARTG entry — Visual identification/product description.</td>
<td>Correction</td>
</tr>
<tr>
<td>CAGN</td>
<td>Correct an ARTG entry — Good name</td>
<td>Correction</td>
</tr>
<tr>
<td>OMPS</td>
<td>Medicines and poisons — scheduling changes</td>
<td>SAR</td>
</tr>
<tr>
<td>OQRC</td>
<td>Quality-related changes (other) that do not create a separate and distinct good.</td>
<td>Category 3</td>
</tr>
</tbody>
</table>
Cell bank or seed lot changes

Self-assessable requests (SARs)
These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989.
The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

CSNW: Cell bank or seed lot — addition of a new working cell bank or working seed lot
Addition of a new working cell bank or working seed lot.

Conditions

- The new working cell bank or working seed lot is to be derived from the previously approved master cell bank or master seed lot.
- The TGA must have explicitly approved the protocol for this purpose. The protocol should have been submitted with the application for registration or a subsequent Category 3 application to change the working cell bank or working seed lot.
- Genetic stability, product yield, adventitious agent safety, and quality and purity must not be affected by the change, as shown by the validation study.

You must submit:

- Details of the new working cell bank or working seed lot.
- The proposed date of implementation.
- A declaration that the new working cell bank or working seed lot has been validated by an approved protocol (stating the date of approval of the protocol) and found to be acceptable.

CSSS: Cell bank or seed lot — change of storage site of master or working cell bank or seed lot
Change to the storage site for the master cell bank or seed lot, or working cell bank or seed lot.

Conditions

- The change must be to the backup/reserve storage site only.

You must submit:

- The address of the new site.
- Details of the facility that has taken responsibility for GMP compliance for the secondary storage site.

Category 3 requests — Data evaluation required under s. 9D(3)
These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

The Category 3 code listed below is broadly representative of the types of quality-related changes that can be submitted under this heading that require the evaluation of data.
CBSL: Cell banks or seed lots — changes

Other quality related changes to cell banks or seed lots (for biological medicines that are not influenza vaccines).

Examples of changes to cell banks and seed lots that require the evaluation of data include:

- The creation of a new master cell bank or seed lot. These may be permitted as a Category 3 application (versus a Category 1 application) only if there is justification for not providing clinical data.
- The creation of a new working cell bank or seed lot (in some circumstances such changes can be self-assessable).
- A change in storage conditions.
- A change in the primary storage site of the cell bank or seed lot – the new site will require GMP clearance.
  - A primary storage site for the master or working cell bank or master or working seed lot is the principal storage site or location from which the master and working cell bank/seed lot is retrieved for use in manufacturing. The site(s) which are used for back-up storage of the master or working cell bank/seed lot are considered secondary storage sites(s).

Conditions

You must submit:

- Details of the proposed change.
- Justification for the change, including changes to test procedures.
- Appropriate validation data.

Other cell bank or seed lot changes

Information about changes to the working seed lot for influenza vaccines is at:

- IVSL: Influenza vaccine — working seed lot change
Drug substance or excipient changes

Certified product details (CPD) documents

For many biological medicines, critical tests are conducted on the drug substance and not repeated on the drug product because of low concentrations of the drug substance or interference by excipients.

If any of the notification requests below result in changes to the drug substance or drug product specifications or the non-pharmacopoeial test methods, please provide a new copy of the entire document, including testing methodology, even if these details have not changed. The CPD document can be provided using the CPD form available on the TGA website.

Changes that do not require reporting to the TGA

These changes can be implemented without notifying the TGA. This does not include any proposed changes that require a consequential change to the approved product information of the registered medicine.

Drug substance and excipients — change to local handling agent contact details (including material of biological origin)

You do not need to notify the TGA if you are making a variation that involves changes to the local distributor of the drug substance and excipient including material of biological origin (same site and method of manufacture, specifications and, where applicable, biological source, including geographical origin and supplier).

Correction to, or completion of, an ARTG entry

Sponsors can request corrections to ARTG entries under s. 9D(1) of the Therapeutic Goods Act 1989. Alternatively, the Secretary can make corrections to ARTG entries under s. 9D(1), at his or her initiative. Refer to the Minor variations to prescription medicines – Process guidance for further information.

CAAO: Correct an ARTG entry — Animal origin

Conditions

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.

CAFC: Correct an ARTG entry — Formulation

Conditions

You must submit:
• Details of the correction or additional information.
• Relevant justification and documentary evidence.
• An assurance that the only changes being made to the ARTG entry are those identified in the request.

Notifications
These variations fall under section 9D(2C) of the *Therapeutic Goods Act 1989*. Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

**ISAM: Drug substance and excipients specifications — change of test method**

Change to test method of the drug substance, where it is replaced with a pharmacopoeial method.

**Conditions**

- The method being changed must not be a viral safety testing method.
- The in-house test method being changed is replaced with a pharmacopoeial method. If there are differences in specifications between the two methods, the more stringent specifications should apply.
- The stringency of the specifications should not decrease as a result of the change.
- Batch analytical data for at least three commercial batches should have been generated to demonstrate compliance with the new test and limit.

You must submit:

- Details of the new method.
- An updated CPD document, if applicable.

**ISNL: Drug substance or excipients specifications — narrowing of limits**

More stringent limits for test results of the drug substance, starting materials, intermediates or excipients in the drug product.

**Conditions**

- The proposed limits must be consistent with the relevant TGA standards and guidelines.
- Do not change the composition of the substance tested. For example, you cannot narrow the test limits for isoelectric point, as this could alter the substance by resulting in the omission of a charge isoform of protein.
- The change must not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a variation application).
- The change must be within the range of currently approved limits.
- The test procedure remains the same, or changes in the test procedure are minor.

You must submit:

- The revised set of specifications for the substance.
ISPT: Drug substance or excipients specifications — amendments resulting from pharmacopoeial or TGO changes

Changes resulting from amendments to pharmacopoeial requirements or the requirements of Therapeutic Goods Orders.

If a substance complies with the requirements of an earlier edition of an official pharmacopoeia, such as the British pharmacopoeia [BP], it would be appropriate to substitute the requirements of the current edition of that pharmacopoeia. However, any tests that were performed in addition to those of the pharmacopoeial monograph should continue to be applied.

Changing from the requirements of one pharmacopoeia to those of another (such as from the USP to the BP) is not covered by this section and may require evaluation of data by the TGA.

Conditions

- The change should not involve changing from the requirements of one pharmacopoeia to those of another.
- Any tests that were performed in addition to those of the pharmacopoeial monograph or TGO must continue to be performed.
- The new pharmacopoeial monograph or amended TGO must be applicable to the substance.

You must submit:

- The revised set of specifications for the drug substance.
- An updated CPD document, if applicable.

Self-assessable requests (SARs)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

IMRS: Drug substance and excipients manufacture (from Category IC ruminant tissues) — changes in source (from animal to non-animal) and/or manufacturing process or site

Change to source, manufacturing process or site of manufacture of excipients derived from Category IC ruminant tissues.

Category IC ruminant tissues are defined in the TGA's Transmissible Spongiform Encephalopathies (TSE): TGA approach to minimising the risk of exposure.
Conditions

- The product must only be intended for oral, topical, vaginal, rectal or inhalation routes, with no potential for cross-contamination with higher risk (Category A or B) tissues.
- The change should be from a ruminant-derived source to a plant or other non-animal source.
- The product should not be administered by the parenteral, ophthalmic or intra-tracheal routes.
- Either no changes to the specification of the excipients have been made, or the excipients have been changed as allowed in the Drug substance or excipient changes section.

You must submit:

- Where relevant, Certificate of Suitability (CEP) issued by the European Directorate for the Quality of Medicines and Healthcare (EDQM) to the manufacturer of the excipient (acceptability of the CEP depends on the source country of the animal and the parts of the animal used to manufacture the excipient).
- A declaration that the Category IC material has been self-assessed and complies with the TGA’s requirements regarding TSE risks.
- An assurance that records of compliance will be maintained for future inspection by the TGA.
- The revised specifications, if changes have been made.

**ISEM: Drug substance and excipients specifications — change to method of analysis of non-biological excipients in a biological medicine**

Change to the method of analysis of non-biological excipients for biological medicine products.

**Conditions**

- The change should only be to a non-pharmacopoeial method of analysis.

If tested according to a pharmacopoeial method, a change to the method of analysis of a non-biological excipient does not require prior approval.

- The change should demonstrably improve precision, accuracy or specificity, without reducing any of these parameters. The one exception is that improved specificity or accuracy may be associated with reduced precision, but only if precision remains within the specified limits.

You must submit:

- Details of the new test method.

You must generate the following:

- Appropriate validation data for the proposed method.

**ISNT: Drug substance and excipients specifications — addition of new test and limit**

Addition of a new test and limit to the existing specifications of the drug substance, starting materials, intermediates or excipients in the drug product.
Conditions

- The test should be relevant.
- The limits proposed should be based on batch analytical data and must comply with any applicable official standard or relevant guidelines.

You must submit:

- Details of the test method.
- The revised set of specifications for the substance.
- The updated CPD document.

You must generate the following:

- Appropriate validation data for the test method.

**ISPE: Drug substance and excipients specifications — minor changes to physicochemical test methods and limits**

Minor changes to physicochemical tests for excipients.

Conditions

- The change should be a minor change to methods for parameters such as pH, osmolality, hydration state, water content or spectrometry. Any other changes require evaluation of supporting data by the TGA.
- The proposed changes should meet pharmacopoeial requirements.
- The proposed changes should not include changes to specifications of excipients.

You must submit:

- A summary description of the change.
- Details of the new method.

**ISQC: Drug substance and excipients specifications — changes to quality control testing equipment**

Change to equipment used for quality control testing of the drug substance, starting materials, intermediates or excipients in the drug product.

Conditions

- The change should meet previously approved validity criteria for the test method. Changes that do not meet previously approved validity criteria are not self-assessable, and the TGA will need to evaluate supporting data.

You must submit:

- Description of the new equipment.
- An updated CPD document, if applicable.

You must generate the following:

- Appropriate validation data for the changed test equipment using the previously approved criteria and, where applicable, the same validation protocol as was used for the previously approved equipment.
• Appropriate validation data for the relevant consumables if the type or brand of consumables used with the equipment is critical (that is, included in the protocol).

**ISRM: Drug substance and excipients specifications — change to method of determining residual solvents (including water)**

Change to the method for determining the content of residual solvents, including water of the drug substance or excipients in the drug product.

**Conditions**

• The new method should demonstrably improve precision, accuracy or specificity, without reducing any of these parameters. The one exception is that improved specificity or accuracy may be associated with reduced precision, but only if precision remains within the specified limits.

You must submit:

• Details of the new method.
• An updated CPD document.

You must generate the following:

• Appropriate validation data for the proposed method.

**Category 3 requests — Data evaluation required under s. 9D(3)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

**IMPC: Ingredients of human and animal origin — source or manufacturing changes**

Changes to the source or manufacturing process of ingredients of human and animal origin.

This includes changes to the source or manufacturing process of raw materials of human or animal origin, for example, albumin or heparin.

**Conditions**

You must submit:

• For excipients derived from Category IC tissues from TSE-relevant ruminant species that are used in products that are implants or injectable products given by the parenteral, ophthalmic or intra-tracheal routes, or for excipients derived from Category IA or IB tissues from TSE-relevant ruminant species (see *Transmissible Spongiform Encephalopathies (TSE): TGA approach to minimising the risk of exposure*) used in products given by the oral, topical, vaginal, rectal or inhalation routes:
  – details of the excipients and the proposed changes
  – measures taken by the manufacturer to minimise TSE risks.

• Refer to TGA’s *Guidance 9* and *Guidance 10* for additional details on requirements for ingredients of human or animal origin. See also *PMFC* and *PFIC* for information about
changes to plasma-derived products. Refer to the information box for special requirements for heparin products.

**PCDC: Ingredients — diluent or product component changes**

Any changes to product components require the TGA to evaluate the data. This includes any changes to diluents and any change to, or addition of, a component of a biological medicine.

**Conditions**

You must submit:

- Description of the proposed change.
- Justification for the proposed change, including changes to test procedures.
- Appropriate validation data.

**GTCM: Gene technology — changes**

Changes to gene technology aspects.

**Conditions**

- Any changes to production cell lines are considered to be major manufacturing changes and will require thorough genetic characterisation, validation, comparability and stability studies.
- If variation in product quality attributes is found, clinical data will probably need to be provided to support the changes. This would require lodgement of a Category 1 application under the streamlined submission process. If there is any doubt about what type of application is required, contact the TGA.

**Category 3 requests — Data evaluation required under s. 23 (separate and distinct good)**

These variations fall under s. 23 of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

**GTCD: Gene technology — including (but not limited to) changes to cell lines**

Any change to production cell lines is considered to be a major manufacturing change and will require thorough genetic characterisation, validation, and comparability and stability studies.

If the product quality varies as a result of the change, clinical data are likely to be needed. This requires lodgement of a Category 1 application under the streamlined submission process. If sponsors have any doubt about the type of application required, they should contact the TGA.

**Conditions**

- Sponsors must revalidate the manufacturing process if there is any change in batch size or batch definition (for example, pooling of multiple batches from fermentation), or a change to the in-process controls.
- Analytical validation will need to be redone if there are any changes to analytical methods or specifications.
Sponsors must submit:

- If you choose not to provide validation, you must include a statement of assurance that there have been no changes to the process, in-process controls, analyses and specifications.
Site of manufacture changes

Definitions

**Change in site of manufacture** means a change in the location of the manufacturing premises.

**Packaging material** means any material employed in the packaging of a medicinal product, excluding any outer packaging used for transportation or shipment:

- Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.
- Secondary packaging includes any packaging or labelling (including repackaging or labelling, over-labelling or supplementary labelling) where the medicine remains in the primary container and that primary container is not opened, breached or modified in the secondary packaging process.
- Primary and secondary packaging require different levels of good manufacturing process certification.

**Release for supply** means that 'medicinal products are not sold or supplied before an authorised person has certified that each production batch has been produced and controlled in accordance with the requirements of the market authorisation and other regulations relevant to the production control and release of medicinal products’ (refer to the Guide to Good Manufacturing Practice for Medicinal Products).

- There may be more than one site involved in release for supply of a product. However, release for supply should only happen once, to ensure that the complete batch records (and responsibility for release) are held in one place. All sites must demonstrate compliance with good manufacturing practice (GMP) through a Therapeutic Goods Administration licence or clearance. Compliance with shipping conditions during importation into Australia is the responsibility of the Australian sponsor for products released for supply overseas. The sponsor does not require a GMP licence to perform this step.

Changes that do not require prior approval

These changes can be implemented before you inform the TGA of the change. Reporting to the TGA should be made in writing, together with any relevant documentary evidence required in support and the date of implementation advised. No specific form is required. This process cannot be used if the proposed changes require a consequential change to the approved product information of the registered medicine.

See guidance on Reporting on changes that do not require TGA approval for further details on the process.
Manufacturing — change to manufacturer’s name or the manufacturing address, provided the actual site location does not change

Change to manufacturer’s name only (including manufacturers who are also product sponsors) or the manufacturing address, provided the actual site location does not change.

Conditions

- The change includes manufacturers who are also product sponsors.
- The physical location of the manufacturing facility remains the same.

You must submit:

- Notification of the change
- Valid evidence of good manufacturing practice (GMP) for the company with the new name.

Manufacturing — changes to the acceptance criteria for raw materials

Changes to the method of manufacture of a drug substance or drug product.

Conditions

- The changes must meet the specifications of the relevant official standard.
- There is no reduction in the quality of the product.

You must submit:

- Written notification of the change, including date of implementation.
- A summary of the new acceptance criteria, preferably in tabular format.
- Any relevant documentary evidence.

Manufacturing — changes to manufacturing process documentation (editorial)

Typographic and editorial changes to documentation for the manufacturing process.

Conditions

- The performance of the procedure has not changed.

You must submit

- Written notification of the change, including date of implementation.
- A clean and a marked-up copy of the manufacturing process documentation.
- Any relevant documentary evidence.

Notifications

These variations fall under section 9D(2C) of the Therapeutic Goods Act 1989.

Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

OAMS: Albumin — change of manufacturer’s name or contact details

Change in details of albumin manufacturer or supplier.
Conditions

- The change may apply to the name or contact details of albumin suppliers or manufacturers, but not to the site or process of manufacture.
  - Changes to site or process of manufacture of albumin products require TGA evaluation of supporting data.

You must submit:

- Details of the new manufacturer or supplier.
- Evidence of GMP clearance, showing the changed name.
- An assurance that the albumin still complies with relevant TGO and other standards such as the European or British Pharmacopoeia (Ph Eur or BP).

**PMRS: Drug product site of manufacture — addition of new site of release-for-supply operations for a registered drug product**

Addition of a new manufacturer for release for supply of the final drug product.

Conditions

- The new site must either have:
  - for Australian manufacturers, a current manufacturing licence issued by the TGA for this type of manufacture or
  - for overseas manufacturers, current GMP clearance issued by the TGA and valid at the time of this application for this type of manufacture.

You must submit:

- Details of the new manufacturing site
- The Australian licence and/or GMP clearance number.

**Self-assessable requests (SARs)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989*.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

**OHMS: Heparin (crude) – change of heparin manufacturer or supplier**

Change in manufacturer or supplier of crude heparin.

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**Heparin products**

The stage of manufacture at which starting material for a heparin product is considered to be the drug substance (also known as the active pharmaceutical ingredient, or API) is earlier than for other biological medicines. This is described in current monographs and good manufacturing practice (GMP) requirements for heparin products. It means that GMP clearance is required earlier in the process for heparin products than for products that do not contain heparin.

The point at which the drug substance starting material is introduced into the
process, as interpreted by the Therapeutic Goods Administration (TGA) for manufacture of a heparin drug substance, is defined in the flowchart below. It is important to note that steps A to B in the flowchart are the only steps in manufacture that do not have to be covered by TGA-issued GMP clearance.

(A) Porcine intestinal mucosa
   ↓
   Extraction
   ↓
   Enzymatic digestion
   ↓
   Ion exchange chromatography
   ↓
   Precipitation
   ↓
   Drying or lyophilisation
   ↓
(B) Drug substance starting material (crude heparin)
   ↓
(C) Heparin drug substance
   ↓
(D) Heparin finished product

Flowchart of the manufacturing process for heparin drug product from porcine intestinal mucosa

Manufacturing steps A to B result in the drug substance starting material (crude heparin). Any step of manufacture beyond this point is regarded as drug substance manufacture and must be covered by TGA-issued GMP clearance.

**Conditions**

- There should be no change to the country of origin of the crude heparin.

You must submit:

- Details of the change, including the following:
  - names and addresses of the supplier(s) of the crude heparin
  - names and addresses of the suppliers of the raw starting material (the porcine intestinal mucosa)
  - names and addresses of the suppliers any of the intermediates up to the crude heparin.

**PDDM: Drug product/substance site of manufacture — cessation of a site or deletion of a manufacturing step**

Deletion of site of manufacture.

**Conditions**

You must submit:

- The name and site address of the manufacturer and the steps of manufacture to be deleted.
- GMP clearance to show that there is at least one validly registered site of manufacture performing the same step(s) of manufacture as the deleted site. This evidence should be in
the form of the current printout from the TGA eBusiness Services website for the product or a copy of the TGA approval.

**PDQC: Drug product/substance site of manufacture — change to quality control testing site**

Change to site of quality control testing.

**Conditions**

- There should be no modifications to the testing procedure, and the previously approved validation criteria should be met.
- The new site must either have:
  - a current manufacturing licence issued by the TGA (Australian manufacturers) for this type of manufacture or
  - a current GMP clearance issued by the TGA and valid at the time of this application (overseas manufacturers) for this type of manufacture.
- There should be no changes to the test methods used for testing the product, whether or not the test methods have been provided to the TGA previously, except where allowed by other sections within this document.
- There should be no impact on existing method validations, and the test methods have been adequately qualified to generate results comparable to that of currently approved quality control sites. The qualification data should be provided to TGA on request.
- The change should not be a change to a viral safety testing site.

You must submit:

- The name and address of the new site.
- Details of the manufacturing step(s) undertaken at the new site of manufacture.
- A copy of the Australian licence and/or GMP clearance.

**PMER: Drug product site of manufacture — change to manufacturer or supplier of excipients or raw materials**

Change to manufacturer or supplier of excipients or raw materials.

**Conditions**

- The change should not be to excipients or raw materials of animal or human origin.
- The change should not be to excipients or raw materials used in heparin products.
- The change should not be to excipients produced by recombinant DNA technology.

You must submit:

- The name and street address of the new manufacturer.
- An assurance that the excipients or raw materials comply with previously approved acceptance criteria and/or storage conditions.
PMSP: Drug product site of manufacture — addition of new manufacturing site for secondary packaging operations

Addition of a new site of secondary packaging operations for an already registered product.

**Conditions**

- The new site must either have:
  - a current manufacturing licence issued by the TGA (Australian manufacturers) for this type of manufacture or
  - a current GMP clearance issued by the TGA and valid at the time of this application (overseas manufacturers) for this type of manufacture.

- Apart from the change in site of manufacture, there should be no changes to any other aspect of the quality data other than changes to manufacturing equipment. Where a change in manufacturing equipment is made, this should have been validated in accordance with the principles of GMP.

You must submit:

- Details of the manufacturing step(s) undertaken at the new site of manufacture.
- A copy of the Australian licence and/or GMP clearance.

**Category 3 requests — Data evaluation required under s. 9D(3)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

**APMS: Manufacturing — changes to the manufacturing site of the drug substance or drug product**

Changes to the site of manufacture of the drug substance and drug product.

**Conditions**

You must submit:

- GMP evidence for the new site (that is, the Australian licence for an Australian site, or a current GMP clearance for an overseas site or reference to the clearance submission number). The Australian licence or GMP clearance should cover the relevant manufacturing steps and must be valid at the time of the request.

- A declaration that the manufacturing process, including batch size, is the same as that used at the currently approved manufacturing site, or a description of any differences between the processes at the new and currently approved sites.

- For plasma products, comparative impurity profiles from representative batches from the current and new sites of manufacture using validated test methods.

- Appropriate validation of the process at the new site (including validation of sterile manufacture and sterilisation processes, if applicable) to demonstrate that the product manufactured at the new site meets the currently registered requirements for in-process controls and the drug product specifications.
- Description and validation of quality control test methods where there is a change in test procedures or where the laboratory testing the product (site of quality control testing) has changed.

- Certificates of analysis for three sequential, preferably full-scale batches of drug product that were manufactured at both the currently approved site and the new site.

- Relevant comparative data on the product (see APMP: Manufacturing — changes to the manufacturing process of a drug substance and drug product).

- Relevant stability data for batches produced at the new site (refer to guidance on Stability testing for prescription medicines).
  - For biological medicine products requiring refrigeration or freezing, stability testing must be in real time at the specified storage temperature, for at least the requested shelf life. The time out of refrigeration (which also includes time out of the freezer) during normal manufacturing processes, up to the point of return to the fridge or freezer following labelling and packaging, should have been defined and justified. From that point onward, all storage and shipping conditions should be justified by the real-time stability data; the data for justifying any temperature excursions should include real-time studies of the proposed excursion followed by return to the normal storage conditions for the remainder of the shelf life.

- If the change is likely to affect critical quality parameters, data from comparability studies on pre-variation and post-variation product.

- Appropriate validation data (including revised viral load reduction claims), where a change is to a process involved in viral reduction.
Drug product manufacture changes

Correction to, or completion of, an ARTG entry

Sponsors can request corrections to ARTG entries under s. 9D(1) of the Therapeutic Goods Act 1989. Alternatively, the Secretary can make corrections to ARTG entries under s. 9D(1), at his or her initiative. Refer to the Minor variations to prescription medicines — Process guidance for further information.

CAMC: Correct an ARTG entry — Manufacturer

Conditions

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.
- Valid GMP clearances and/or Australian manufacturing licences for the relevant steps of manufacture.

Self-assessable requests (SARs)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989. The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

PMDS: Drug product manufacture — changes to dimensions, shape, inked imprint, embossing or debossing of solid dosage forms

Changes to dimensions, shape, inked imprint, or embossing and debossing of solid dosage forms.

Definitions

An inked imprint is a marking or pattern on the product made by printing with an ink during product manufacture.

Embossing/debossing is either the raised (embossed) or depressed (debossed) marking, pattern or engraving on the product that is formed by special tools used during product manufacture.

Conditions

- The product should be a solid dosage form (note that capsules are considered to be solid dosage forms, but impregnated sponges are not).
- There should be no concurrent change to the formulation except as allowed in self-assessable requests that create a separate and distinct good.
- There should be no change to, or addition or deletion of, scoring.
- Where an inked imprint is changed, there should be no change to the imprinting ink used.
You must submit:

- The new product description.
- The revised set of drug product specifications at release and expiry.
- An updated CPD document.
- Where the proposed change requires an update to the PI, details of changes to the PI, as outlined in the Minor variations to prescription medicines – Process guidance.

**PMRO: Drug product manufacture — reduction or removal of API and excipient overages for ingredients that are not antioxidants or similar**

Reduction or removal of overage.

**Conditions**

- Stability testing of the product with reduced overage on at least three production batches of the post-variation product should show that all products meet specifications at the expiration date. This should be done according to International Conference on Harmonisation (ICH) requirements, and data should be made available to the TGA on request.

  Any failure to meet drug product specifications during the stability trials should be notified to the TGA as a priority. The TGA reserves the right to withdraw the product from the market if this requirement is not met.

- Any excipient involved should not be an antioxidant or another ingredient whose function (at least in part) involves being ‘consumed’ over time.

You must submit:

- The revised manufacturing formula.
- An updated CPD document.

You must generate the following data:

- Appropriate validation data for manufacture of the product with reduced overage.

**Category 3 requests — Data evaluation required under s. 9D(3)**

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

**APMP: Manufacturing — changes to the manufacturing process of a drug substance and drug product**

Changes to the method of manufacture of the drug substance and drug product.
Conditions

You must submit:

- A detailed description of the changed manufacturing process, including a flow diagram.
- Process validation data for the changed process (including validation of sterile manufacture and sterilisation processes, if applicable).
- If the drug substance is made entirely by fermentation, details of any material of animal origin used during the process that is classified as Category IC in the TGA’s Transmissible Spongiform Encephalopathies (TSE): TGA approach to minimising the risk of exposure. If appropriate, provide the necessary assurance regarding self-assessment of TSE risks of such materials.
- Where a manufacturer produces multiple products at the same site, details of the manufacturing process(es) and the measures taken to ensure that there is no cross-contamination of different drug substances.
- Batch analytical data generated for three full production-scale batches of drug substance or drug product manufactured using the proposed process, unless otherwise justified. These data should be compared with data from at least three batches of recently manufactured pre-variation product and the mean, standard deviation and range of historical data. All data should be generated using approved routine quality control methods, unless otherwise justified and details are provided of the non-routine methods used.
- Real-time stability data generated for batches produced using the new process (refer to guidance on Stability testing for prescription medicines).
  - For biological medicine products requiring refrigeration or freezing, stability testing should be in real time at the specified storage temperature, for at least the requested shelf life. The time out of refrigeration (which also includes time out of the freezer) during normal manufacturing processes, up to the point of return to the fridge or freezer following labelling and packaging, should have been defined and justified. From that point onward, all storage and shipping conditions should be justified by the real-time stability data; the data for justifying any temperature excursions should include real-time studies of the proposed excursion followed by return to the normal storage conditions for the remainder of the shelf life.
- If the changes proposed are to the drug product and may affect bioavailability of the product, comparative bioavailability data.
  - If bioavailability data are required and are submitted to support the change, the application becomes a Category 1 application.
- If the change is likely to affect critical quality parameters, data from comparability studies on pre-variation and post-variation drug substance or drug product.
- If the change is approved, an updated CPD document.
- Appropriate validation data (including revised viral load reduction claims), where a change is to a process involved in viral reduction.
Drug product specifications or test changes

Certified product details (CPD) documents
For many biological medicines, critical tests are conducted on the drug substance and not repeated on the drug product because of low concentrations of the drug substance or interference by excipients.

If any of the notification requests below result in changes to the drug substance or drug product specifications or the non-pharmacopoeial test methods, please provide a new copy of the entire document, including testing methodology, even if these details have not changed. The CPD document can be provided using the CPD form available on the TGA website.

Notifications
These variations fall under section 9D(2C) of the Therapeutic Goods Act 1989. Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

PMPL: Drug product specification — minor changes to physicochemical test methods and limits
Minor changes to physicochemical tests.

Conditions
- There is no change in test method other than minor changes to existing test methods for physicochemical parameters of the drug product such as pH, density, specific gravity, optical rotation, extractable volume, osmolality, osmolarity or viscosity.
- The test limit must either remain unchanged or be more stringent.

You must submit:
- A summary description of the change, and details of the new method.
- An updated CPD document.

You must generate the following data:
- Appropriate validation data demonstrating the new test is at least equivalent to former procedure.

PSNL: Drug product specification — narrowing of test limits
Revision of the approved specifications for testing of the final drug product, to make the limits applied to test results more stringent.

Conditions
- The new limits must be either the same as, or more stringent than, any applicable standard or guidelines.

You must submit:
• The revised set of specifications.

**PSNT: Drug product specification — addition of test and limit**

Addition of a new test and limit to the existing specifications.

**Conditions**

• The additional test must have been previously evaluated by the TGA.

• The proposed limit (release and expiry) should be based on batch analytical data and should comply with, or be more stringent than, any applicable official standard or relevant accepted guidelines for such a test.

• The test method should only be used at a registered quality control testing site that has appropriate GMP clearance.

You must submit:

• Details of the new test method.

• The revised set of drug product specifications (release and expiry).

• An updated CPD document.

You must generate the following data:

• Appropriate validation data for the new test method.

**PSPT: Drug product specification — changes resulting from amendments to a TGO or pharmacopoeial requirement.**

Changes resulting from amendments to pharmacopoeial requirements or the requirements of Therapeutic Goods Orders.

**Conditions**

• The new pharmacopoeial monograph or TGO should be suitable for the product.

• The change must not involve changing from the requirements of one pharmacopoeia to those of another.

• Any tests that are performed in addition to those of the pharmacopoeial monograph or TGO must continue to be performed.

• The test method must only be used at a registered quality control testing site that has appropriate GMP clearance.

• If the change involves updating microbiological test requirements for non-sterile products to meet TGO No. 77—Microbiological standards for medicines, the product should have undergone a risk assessment for objectionable microorganisms, in addition to those specified in the pharmacopoeias that form the basis of TGO 77.

• The change must not be a consequence of any commitment from previous assessments to review specification limits (e.g. made during the procedure for the marketing authorisation application or a variation application) unless the supporting documentation has been already assessed and approved within another procedure.

• The change must not result from unexpected events arising during manufacture e.g. new unqualified impurity; change in total impurity limits.

• The change must be within the range of currently approved limits.

• The test procedure must remain the same, or the changes in the test procedure are minor.
You must submit:

- The revised set of drug product specifications (release and expiry).
- An updated CPD document.
- For updating microbiological test requirements for non-sterile products to meet TGO No. 77, an assurance that the report of the risk assessment for objectionable microorganisms is available for review, if required by the TGA.

You must generate the following data:

- Appropriate validation data must have been generated where applicable.

**PSQC: Drug product specification — change to quality control testing equipment**

Changes to equipment used for quality control testing of the final drug product (including sterility, microbiological, chemical, physical and bacterial endotoxin or pyrogen testing).

**Conditions**

- The change must meet any previously approved test method validity criteria.

You must submit:

- A description of the new equipment.
- An updated CPD document.

You must generate the following data:

- Appropriate validation data must have been generated for the changed equipment using the previously approved criteria and, where applicable, the same validation protocol as was used for the previously approved equipment.
- If the type or brand of consumables used with the equipment is critical (that is, included in the protocol), appropriate validation data must also be generated for the relevant consumables.

**Self-assessable requests (SARs)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989*.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

**PSSM: Drug product specification — change to sterility test method**

Change to sterility test method.

**Conditions**

- All aspects of the test are in accordance with the requirements of the internationally harmonised test published in the BP, Ph. Eur. or USP and as specified in TGO 77—Microbiological Standards for Medicines.
- The test follows the guidelines on particular aspects of the sterility test in Guidance 17—Microbial quality of prescription and over-the-counter medicines.

You must submit:
• Details of the new test method.
• An updated CPD document.
You must generate the following data:
• Comparative batch data using validated test methods.

Self-assessable requests (SARs) that create a separate and distinct good (s. 23)

These variations fall under s. 23 of the Therapeutic Goods Act 1989. These are self-assessable requests that create a separate and distinct good and the existing AUST R number can be retained under the provisions of the Therapeutic Goods (Groups) Order No. 1 of 2001.

All other formulation changes require the submission of data and a new entry on the ARTG.

DFCI: Inked imprint – addition, deletion or variation

Inked imprints on a solid oral dosage form may be added, deleted or varied through self-assessment.

If the proposed change is to the inking pattern, but the same ink is used, this represents a change to an existing ARTG entry — see PMDS: Drug product manufacture — changes to dimensions, shape, inked imprint, embossing or debossing of solid dosage forms.

Conditions

• Any new colour or dye of an ink should be listed in the current TGA list of colours permitted for use in medicines for ingestion (see Colourings used in medicines for topical and oral use), and should comply with the specifications in that list.
• Any new proprietary excipient to be used should be already entered in the ARTG.
• If relevant, the drug product specification should be revised to incorporate any change in product description.

You must submit:

• A comparative list of the current and new product formulations, if relevant.
• Information on use or non-use of human embryos or human embryonic stem cells, or other material sourced from human embryos or human embryonic stem cells, in the manufacture of the product (this is a requirement under Regulation 9B of the Therapeutic Goods Regulations 1990).
• The revised product description (if this has changed), incorporated into the revised set of drug product specifications (release and expiry).
• The PI number for the proprietary excipient, if relevant, together with its ARTG number.
• An updated CPD document for the product that incorporates the changes, if applicable.
• A clean copy of the PI must be provided. Where the proposed change would involve approval of a new PI, a marked-up copy should also be provided.

DFFC: Formulation — change of colouring agent, flavour or fragrance

Certain changes to, or addition or deletion of, colouring agents, flavour or fragrance of a product may be made through self-assessment.
Conditions

- The colouring agent, fragrance or flavour is present in the formulation at not more than 2% w/w or w/v.
- Any new colour is listed in the current TGA list of colours permitted in medicines for oral use, and complies with the specifications in the same list (see Colourings used in medicines for topical and oral use).
- Any new proprietary excipient to be used should be already included in an ARTG entry.
- If relevant, the drug product specifications (release and expiry) should be revised to incorporate any new product description or other organoleptic properties of the product.

You must submit:

- The proprietary ingredient number for the new proprietary excipient, together with the ARTG number of the existing good, if relevant.
- A comparative list of the current and new product formulations.
- Information on use or non-use of human embryos or human embryonic stem cells, or other material sourced from human embryos or human embryonic stem cells, in the manufacture of the product (this is a requirement under Regulation 9B of the Therapeutic Goods Regulations 1990).
- An updated CPD document for the product that incorporates the changes, if applicable.
- A clean copy of the PI must be provided. Where the proposed change would involve approval of a new PI, a marked-up copy should also be provided.

You must generate the following data:

- Relevant comparative data of the type listed below should have been generated for the dosage form manufactured using the new and old formulations.
- At least three recently manufactured batches of the pre-variation product and one production batch of the post-variation product should be tested, preferably at the same time and using the same method. The second and third batches manufactured under the new conditions, if not available at the time of application, should be tested, and the results should be reviewed by the sponsor as soon as they become available. The TGA should be notified of any differences as a priority. The following data (where applicable) is to be provided for each batch of the product to be tested:
  - All solid dosage forms (for example, tablets, capsules, compressed suppositories and pessaries) must have similar comparative dissolution profiles — that is, the similarity factor, \( f_2 \), should be between 50 and 100. These data are not required if the API is in solution at any stage during manufacture of the drug product, or if it is in solution in the drug product or present as liquid globules.
  - For semi-solid and liquid products (for example, ointments, creams, lotions, oral liquids, moulded suppositories and pessaries), comparative batch data using appropriate methodology should demonstrate that there has been no change to the particle size distribution and polymorphic form of the drug substance in suspension. These data are not required if the drug substance is in solution at any stage during manufacture of the drug product, or if it is in solution in the drug product or present as liquid globules.
- A stability test on the reformulated product should have begun on at least one production-scale batch, and should begin on the second and third batches as they become available. If the results of the stability test do not meet the specifications, the TGA should be notified immediately, and the reformulated product may be withdrawn from the market at the TGA’s discretion.
Category 3 requests — Data evaluation required under s. 9D(3)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

**IPCS: Drug substance and drug product — changes to specifications or test methods**

This includes changes to, or removal of, a test method, or changes to specifications, where these are not self-assessable changes.

**Conditions**

You must submit:

- A copy of the revised specifications; where relevant, this should be consolidated to apply to all sites of drug substance manufacture.
- Justification for the proposed changes, including any changes to test procedures. Data demonstrating the equivalence of the alternative and/or pharmacopoeial methods may also be required, if relevant.
- Validation of any changed test procedures (including microbiological tests, if applicable).
- Certificates of analysis for three representative batches (preferably sequential batches) of the bulk drug substance or drug product, demonstrating the manufacturer’s ability to meet the revised specifications. Where the expiry specifications change, stability data may be necessary.
- If the change is approved, an updated CPD document.

Category 3 requests — Data evaluation required under s. 23 (separate and distinct good)

These variations fall under s. 23 of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

**PFCF: Formulation — changes**

Some minor formulation changes with no clinical impact may be submitted as a Category 3 application.

However, many changes to the formulation of a biological medicine require evaluation of clinical and nonclinical data. These types of variations should be submitted as Category 1 applications.

Please contact the TGA if you are unsure whether your change meets the criteria for a Category 3 request.
In-house reference standard changes

Notifications

These variations fall under section 9D(2C) of the *Therapeutic Goods Act 1989*.

Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

IRSR: In-house reference standard — replacement

Replacement of an in-house reference standard.

**Conditions**

- The TGA should have explicitly approved the protocol and acceptance criteria including traceability for establishing a replacement standard. The protocol should have been submitted with the application for registration or a subsequent [Category 3 application to change the in-house reference standard](#). This also includes a change in shelf life of the reference standard.

You must submit:

- Details of the new reference standard, including assigned values.
- The reference to the TGA approval of the protocol (that is, TGA submission number).
- The proposed date of implementation.
- An updated CPD document.

Category 3 requests — Data evaluation required under s. 9D(3)

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

IRNA: In-house reference standard — changes

Changes to in-house reference standards.

This applies to the introduction of a new reference standard (that is, a reference standard that has not been previously approved by the TGA) or an additional reference standard.

**Conditions**

You must submit:

- Description of the proposed change.
- Justification for the proposed change, including changes to test procedures.
- Appropriate validation data.
- If the change is approved, an updated CPD document, if relevant.
Purification process changes

Notifications

These variations fall under section 9D(2C) of the *Therapeutic Goods Act 1989*.

Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

PPCR: Purification process — column life reduction

Reduction in the approved column life for columns used in the purification process.

**Conditions**

You must submit:

- A scientific justification for the column life reduction.

PPHR: Purification process — holding time reduction for a non-plasma-derived product

Reduction in the holding time for the drug substance, or intermediates created during manufacture of the drug substance, where the final drug product is non-plasma derived.

**Conditions**

You must submit:

- A scientific justification for the holding time reduction.

Other purification process changes

Other purification process changes require the TGA to evaluate data. See:

- [APMP: Manufacturing — changes to the manufacturing process of a drug substance and drug product](#)
Filling changes

Self-assessable requests (SARs)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989. The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

FLIS: Filling — introduction of a similar filling line

Introduction of a similar filling line.

Conditions

- The new filling line should be similar to the existing filling line.
- There should be no modifications to the procedure, and the previously approved validation criteria (including validated aseptic holding and filling times) and/or release specifications should be met.
- This can include upgrades to an existing filling line.

You must submit:

- General details of the new/upgraded filling line.

Category 3 requests — Data evaluation required under s. 9D(3)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

PFCP: Filling — changes to drug product filling

The types of changes to filling processes for which evaluation of data is required include:

- change to in-process controls
- change in filling equipment that involves use of equipment significantly different from that used previously and that does not involve upgrade of an existing filling line
- increase in filling time.

Conditions

You must submit:

- Description of the proposed change.
- Justification for the proposed change, including changes to test procedures.
- Appropriate validation data.
- If the drug substance is sterile and undergoes no further sterilisation, supporting data for changes to filling time or storage of sterile bulk drug substance. Appropriate validation data to support an increase in filling time should be provided.
Changes to storage of drug substance

Notifications
These variations fall under section 9D(2C) of the *Therapeutic Goods Act 1989*.

Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

**ASRS: API storage conditions — reduction in shelf life**
Reduction in shelf life.

**Conditions**
- The change must not be due to unexpected events arising during manufacture or because of stability concerns.

You must submit:
- Details of the new shelf life.
- A reason for the planned reduction in shelf life.

Self-assessable requests (SARs)
These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989*.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

**ACDM: API storage conditions — change of storage container dimensions or manufacturer**
Change in dimensions or manufacturer of storage container.

**Conditions**
- The surface area in contact with the product should not change.
- The dimensions of the storage container should only increase by 50% or less.
- There should be no change to the container material.

You must submit:
- Details of the change.
- Justification for the change.
- An assurance that stability studies have been conducted.

Category 3 requests — Data evaluation required under s. 9D(3)
These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.
**DDSL: Shelf life — changes to shelf life or storage conditions of the drug substance**

Changes to the shelf life or storage conditions of the drug substance or drug product.

**Conditions**

You must submit:

- Real-time stability data on at least three production-scale batches to support the change. Data from fewer batches or pilot-scale batches may be acceptable, if justified. Shelf life will not be assigned based on accelerated testing.

- If the change is approved, an updated [CPD document where applicable](#).
Changes to storage of drug product

Stability testing

For biological medicine products requiring refrigeration or freezing, stability testing should be in real time at the specified storage temperature, for at least the requested shelf life.

The time out of refrigeration (which also includes time out of the freezer) during normal manufacturing processes, up to the point of return to the fridge or freezer following labelling and packaging, should have been defined and justified. This should be based on worst-case storage scenarios and include storage conditions inherent in the manufacturing process and transport.

From that point onward, all storage and shipping conditions should be justified by the real-time stability data:

- The data for justifying any temperature excursions should include real-time studies of the proposed excursion followed by return to the normal storage conditions for the remainder of the shelf life.

Refer to guidance on Stability testing for prescription medicines for requirements for stability testing of biological medicines.

Correction to, or completion of, an ARTG entry

Sponsors can request corrections to ARTG entries under s. 9D(1) of the Therapeutic Goods Act 1989. Alternatively, the Secretary can make corrections to ARTG entries under s. 9D(1), at his or her initiative. Refer to the Minor variations to prescription medicines – Process guidance for further information.

CASL: Shelf life / storage condition

Conditions

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.

Notifications

These variations fall under section 9D(2C) of the Therapeutic Goods Act 1989.

Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.
PSLD: Drug product storage conditions — reduction in shelf life

Reduction in shelf life.

**Conditions**

- The change must not be due to unexpected events arising during manufacture or because of stability concerns.

You must submit:

- Details of the new shelf life.
- A reason for the reduction in shelf life.

PSET: Drug product storage conditions — changes to excursion temperature during manufacture

Changes to excursion temperature during manufacture.

**Conditions**

- The change is one of the following:
  - a removal of an excursion temperature
  - a reduction in the time spent out of refrigeration, including time out of the freezer.
- All other changes to the excursion temperature require the TGA to evaluate the data. See PSLC: Shelf life — changes to shelf life or storage conditions of a drug product.

You must submit:

- Details of the change.

PSAR: Drug product storage conditions — Addition of a restrictive shelf life or storage condition

Addition of a restrictive shelf life or storage condition.

**Conditions**

- The change must be to a more restrictive shelf life or storage conditions.

You must submit:

- Details of the change.
- The reason for the change.

**Category 3 requests — Data evaluation required under s. 9D(3)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.
PSLC: Shelf life — changes to shelf life or storage conditions of a drug product

Changes to the shelf life or storage conditions of the drug substance or drug product.

Conditions

You must submit:

- Real-time stability data on at least three production-scale batches to support the change. Data from fewer batches or pilot-scale batches may be acceptable, if justified. Shelf life will not be assigned based on accelerated testing.

- For multi-dose products (drug product only):
  - Results of antimicrobial preservative efficacy testing, in accordance with the requirements of TGO 77: Microbiological Standards for Medicines, to support changes to the closed shelf life.
  - Results of simulated in-use testing to support changes to the open in-use shelf life. Details on this testing are provided in Guidance 17: Microbial quality of prescription and over-the-counter medicines.

- For drug products that are to be reconstituted or diluted before use, data to support changes in the storage periods and conditions if the conditions are specified to be longer than 24 hours at 2–8°C or 6 hours at room temperature:
  - Appropriate microbiological data consists of microbiological challenge experiments similar to preservative efficacy testing. Ideally, the results should show evidence of microbial death, but demonstration of stasis (that is, not more than 0.5 log_{10} units higher than the initial value of the inoculum) over the proposed storage period is the minimum requirement.
  - Chemical and physical data showing the stability of the reconstituted product are also required.

- Revised labelling for drug products, if the storage conditions are to be changed.

- Where the proposed change to a drug product would involve approval of an amended PI, details of the amended PI, as outlined in the Minor variations to prescription medicines — Process guidance.

- If the change is approved, an updated CPD document
Fermentation process changes

Notifications

These variations fall under section 9D(2C) of the Therapeutic Goods Act 1989. Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

FPFM: Fermentation — change of filter manufacturer

Change to the manufacturer of the filter used in the fermentation process.

Conditions

- Do not change the internal process controls.
- Do not use the filter for steps that require viral safety validation.
- The new filter meets the same acceptance criteria as the previous filter.
- The new internal process controls for the filtrate have not been changed.

You must submit:

- The reason for the change.
- The new manufacturer’s details.

FPNC: Fermentation — more stringent internal process controls

Introduction of more stringent internal controls on the fermentation process.

Conditions

- Do not change the quality characteristics of the product.

You must submit:

- The reason for the change.
- Details of the new internal process controls.

FPRP: Fermentation — reduction in fermentation period

Reduction in the fermentation period, i.e. the time required to culture and harvest the cell line.

Conditions

- Reducing the fermentation period must not change the batch size.
- Do not change the internal process controls.

You must submit:

- The reason for the change.
- Details of the change.
Other fermentation process changes

Other fermentation process changes require the TGA to evaluate data. See:

- APMP: Manufacturing — changes to the manufacturing process of a drug substance and drug product.
Plasma Master File changes

Changes that do not require prior approval

These changes can be implemented before you inform the TGA of the change. Reporting to the TGA should be made in writing, together with any relevant documentary evidence required in support and the date of implementation advised. No specific form is required. This process cannot be used if the proposed changes require a consequential change to the approved product information of the registered medicine.

See guidance on Reporting on changes that do not require TGA approval for further details on the process.

Plasma - master file changes

The following changes are included in annual updates to plasma master files and therefore do not require separate notification to the TGA:

- addition or removal of collection centres for a currently approved collection organisation (see Guidance 9: Therapeutic goods that contain or are produced from human blood or plasma)
- change of sites for testing of individual donations.
- change of tests for testing individual donations.

Category 3 requests — Data evaluation required under s. 9D(3)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

PMFC: Plasma — master file changes

Other changes to plasma master files. This section also applies to albumin when it is used as an excipient. The format of the plasma master file should comply with the EMA guidance document EMEA/CPMP/BWP/3794/03 Guideline on the Scientific Data Requirements for a Plasma Master File (PMF), which has been adopted by the TGA.

Conditions

Evaluation of data by the TGA is required for the following types of changes:

- country of origin of plasma
- include a new organisation acting as a supplier of plasma (addition of a new collection site within an organisation can be provided in the PMF annual update)
- tests and site of viral testing of manufacturing plasma pool
- manufacturing pool size or number of donations per pool
- hold times for plasma
- donor selection/exclusion criteria
- donation quarantine period.

You must submit:

- Description of the proposed change.
• Justification for the proposed change, including changes to test procedures.
• Appropriate validation data.
Plasma fractionation intermediates changes

Notifications

These variations fall under section 9D(2C) of the *Therapeutic Goods Act 1989*.

Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

**PFCR: Plasma — changes to fractionation intermediates — column life reduction**

Reduction in the approved column life for columns used in plasma fractionation.

**Conditions**

You must submit:

- Details of the change.
- A justification for the proposed reduction.

**PFSC: Plasma — changes to fractionation intermediates — more stringent internal process control**

Introduction of more stringent internal controls on the plasma fractionation process.

**Conditions**

- Do not change the quality characteristics of the product.

You must submit:

- Details of the change.
- The reason for the change.

**Category 3 requests — Data evaluation required under s. 9D(3)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

**PFIC: Plasma — changes to fractionation intermediates**

Examples of types of changes to plasma fractionation intermediates that require evaluation of data by the TGA include changes to:

- filter manufacturer
- batch size
- increase in hold times
- equipment
- addition or deletion of, or change to, a step
• increase in column life
• shelf life for storage of intermediate
• manufacturer (for example, alternative supplier of an intermediate, with no change in the method of fractionation).

A change in the method of fractionation may require supporting clinical data, and would be a Category 1 application

**Conditions**

You must submit:

• Description of the proposed change.
• Justification for the proposed change, including changes to test procedures.
• Appropriate validation data.
Product information (PI) changes

Correction to, or completion of, an ARTG entry

Sponsors can request corrections to ARTG entries under s. 9D(1) of the *Therapeutic Goods Act 1989*. Alternatively, the Secretary can make corrections to ARTG entries under s. 9D(1), at their initiative. Refer to the Minor variations to prescription medicines — Process guidance for further information.

**CAPI: Product Information (PI)**

**Conditions**

- The correction does not involve subsection 9D(2) and subsection 9D(3) changes to the PI.

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.
- A clean and marked-up copy of the draft revised PI.

Minor editorial changes to the product information under s. 9D(3)

This variation falls under s. 9D(3) of the *Therapeutic Goods Act 1989*.

**Minor editorial changes to the product information under s. 9D(3)**

In some cases, the only proposed variation to an ARTG entry is a change to the PI. Most of these changes do not meet the criteria of a safety-related request or self-assessable request above. These are instead processed as minor editorial changes.

**PIME: PI — Make minor editorial changes**

**Conditions**

- The only changes being requested are those identified under this request.

You must submit:

- A clean and marked-up copy of the draft revised PI is provided.
- Details of the safety-related request are provided.
- A justification for the proposed variation is provided.
Self-assessable requests (SARs)

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989*.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

**PIAE: PI — adding the names of excipients in the product**

Adding the names of excipients in the product, whether or not those excipients are referred to in the TGO pertaining to labels.

**Conditions**

- Any included technical information should be accurate and should be obtained from recognised reference sources.
- All names and terminology used in the PI should be Australian approved names or entered in the TGA eBusiness Services code tables.
- Products should not be supplied with a new PI until the change has come into effect.
- The approved amended PI should be updated on the TGA website when the proposed changes come into effect.

You must submit:

- Details of changes to the PI, as outlined in the *Minor variations to prescription medicines* — Process guidance. If the amendments are necessary because of other regulatory actions that have already been approved or notified, evidence of such approval or notification.

**PICA: PI — adding the Chemical Abstracts Service (CAS) number, molecular formula/weight and/or chemical structure/nomenclature of the API**

Adding the Chemical Abstracts Service (CAS) number, chemical structure, molecular formula, molecular weight and/or chemical name/nomenclature of the API.

**Conditions**

- Any included technical information should be accurate and should be obtained from recognised reference sources.
- All names and terminology used in the PI should be Australian approved names or entered in the TGA eBusiness Services code tables.
- Products should not be supplied with a new PI until the change has come into effect.
- The approved amended PI should be updated on the TGA website when the proposed changes come into effect.

You must submit:

- Details of changes to the PI, as outlined in the *Minor variations to prescription medicines* — Process guidance. If the amendments are necessary because of other regulatory actions that have already been approved or notified, evidence of such approval or notification.
PIPD: PI — changing the PI of radiopharmaceuticals to give instructions that the patient dose should be measured immediately before administration

**Conditions**

- Any included technical information should be accurate and should be obtained from recognised reference sources.
- All names and terminology used in the PI should be Australian approved names or entered in the TGA eBusiness Services code tables.
- Products should not be supplied with a new PI until the change has come into effect.
- The approved amended PI should be updated on the TGA website when the proposed changes come into effect.

You must submit:

- Details of changes to the PI, as outlined in the [Minor variations to prescription medicines — Process guidance](#). If the amendments are necessary because of other regulatory actions that have already been approved or notified, evidence of such approval or notification.

PIPS: PI — changing the name, address or other details of the product’s sponsor or distributor

**Conditions**

- Any included technical information should be accurate and should be obtained from recognised reference sources.
- All names and terminology used in the PI should be Australian approved names or entered in the TGA eBusiness Services code tables.
- Products should not be supplied with a new PI until the change has come into effect.
- The approved amended PI should be updated on the TGA website when the proposed changes come into effect.

You must submit:

- Details of changes to the PI, as outlined in the [Minor variations to prescription medicines — Process guidance](#). If the amendments are necessary because of other regulatory actions that have already been approved or notified, evidence of such approval or notification.

PIRI: PI — changing the PI of radiopharmaceuticals to give instructions/information on radiation protection and safety of user and patient.

These may include radiation shielding data, decay charts, procedures to minimise radiation doses to staff and unintended doses to patients, and references to guidelines and codes of practice relating to radiation protection.

**Conditions**

- Any included technical information should be accurate and should be obtained from recognised reference sources.
- All names and terminology used in the PI should be Australian approved names or entered in the TGA eBusiness Services code tables.
- Products should not be supplied with a new PI until the change has come into effect.
• The approved amended PI should be updated on the TGA website when the proposed changes come into effect.

You must submit:

• Details of changes to the PI, as outlined in the Minor variations to prescription medicines — Process guidance. If the amendments are necessary because of other regulatory actions that have already been approved or notified, evidence of such approval or notification.

**PISR: PI — putting into effect the guidelines in section 20.2 of Guidance 20: Radiopharmaceuticals**

**Conditions**

• Any included technical information should be accurate and should be obtained from recognised reference sources.

• All names and terminology used in the PI should be Australian approved names or entered in the TGA eBusiness Services code tables.

• Products should not be supplied with a new PI until the change has come into effect.

• The approved amended PI should be updated on the TGA website when the proposed changes come into effect.

You must submit:

• Details of changes to the PI, as outlined in the Minor variations to prescription medicines — Process guidance. If the amendments are necessary because of other regulatory actions that have already been approved or notified, evidence of such approval or notification.

**Safety-related requests (SRRs)**

These variations fall under s. 9D(2) of the Therapeutic Goods Act 1989.

Requests are assessed on a case-by-case basis and the proposed variation must meet the criteria of being safety-related. Sponsors should be able to justify how a request meets these criteria. Safety-related variations always require changes to the product information (PI).

**PIID: PI — Remove an indication with data**

**Conditions**

• The only changes being requested are those identified under this request.

You must submit:

• A clean and marked-up copy of the draft revised PI.

• Details of the safety-related request.

• A justification for the proposed variation.

**PIIN: PI — Remove an indication — no data**

**Conditions**

• The only changes being requested are those identified under this request.

You must submit:

• A clean and marked-up copy of the draft revised PI.
Details of the safety-related request.

A justification for the proposed variation.

**PIOD: PI — Make safety related changes with data**

**Conditions**

- The only changes being requested are those identified under this request.

You must submit:

- A clean and marked-up copy of the draft revised PI.
- Details of the safety-related request.
- A justification for the proposed variation.

**PION: PI — Make safety related changes no data**

**Conditions**

- The only changes being requested are those identified under this request.

You must submit:

- A clean and marked-up copy of the draft revised PI.
- Details of the safety-related request.
- A justification for the proposed variation.

**Category 3 requests — Data evaluation required under s. 9D(3)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

**PICC: PI — changes to quality aspects of the product information**

**Conditions**

- This variation covers all quality-related changes to the ARTG entry resulting in changes to the PI that are not described above.

You must submit:

- A description of the proposed changes to the PI.
- Details of changes to the PI, as outlined in the [Minor variations to prescription medicines — Process guidance](#).
- Relevant technical data to support the proposed change(s).
Product label changes

Requirements for labels
Mandatory labelling requirements for prescription medicines are set out in the Therapeutic Goods Order (TGO) that pertains to labels, as amended from time to time. It is the sponsor’s responsibility to ensure that their product labels meet any state and territory government requirements.

Changes that do not require reporting to the TGA

This change can be implemented without notifying the TGA. This does not include any proposed changes that require a consequential change to the approved product information of the registered medicine.

You do not need to notify the TGA if you are making the following variations to a label:

- change to AUST R number following an approved change that requires a new AUST R number
- inclusion or removal of, or changes to, sponsor or supplier telephone/facsimile number, email address, barcodes, ABN or Australian Company Number, product code number, patent number, recycle logo and associated text, trademark and other such symbols
- inclusion or removal of date of manufacture of product
- inclusion or removal of foreign national registration number
- changes to colours of artwork
- inclusion or removal of, or changes to, name and address of supplier in New Zealand
- change of typeface and increase in font size of print only
- change in web address, without a change in the content of the website

Conditions

- There must be strictly no other changes and the minimum letter height requirements of the therapeutic goods order pertaining to labels are still observed.
- A change to barcodes may include 2-D matrix codes but not quick response [QR] codes.
- Other symbols that may be changed include ®, © and ™.
- Any change to the colours of artwork must be made without impairing legibility of labels (and unless colour-coding is used to indicate product strength).

Notifications

These variations fall under section 9D(2C) of the Therapeutic Goods Act 1989.

Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.
LPCL: Label — addition or deletion of, or change to, the company logo or livery

Conditions

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

LPCP: Label — addition or deletion of, or change to, the pictogram of a product or its dosage form

Conditions

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.
- The addition or change of a pictogram of a product or its dosage form must only be designed to clarify information about the medicine which is useful for the patient, to the exclusion of any element of a promotional nature
- The change must not involve removal of information relating to the safe use of the product.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

LPCS: Label — addition or deletion of, or change to, the name or address of the Australian sponsor or supplier of the product

Conditions

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.
- The new name or address must be the same as amended on the register.

You must submit:
• Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

LPDG: Label — deletion of existing graphics, pictures or diagrams, and any associated text

Conditions

• There must be no other changes to the label made under this change request.
• The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.
• The change must not involve removal of information relating to the safe use of the product.

You must submit:

• Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

LPDR: Label — deletion of repeated text (present elsewhere on a label) from selected side panels provided that the information is not mandatory

Conditions

• There must be no other changes to the label made under this change request.
• The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

• Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

LPIA: Label — addition of simple instructional/informational/anti-tampering statements, or information about a changed appearance of the dosage form

Conditions

• There must be no other changes to the label made under this change request.
• The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.
You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

**LPOP: Label — addition or deletion of, or change to, label text of outer protective pouches or overwraps of the container or primary pack**

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.
- The new text must not be confusing, promotional or contradictory to text on the container or primary pack labels

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

**Self-assessable requests (SARs)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989*.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

**LOAI: Label — addition of a new TGA-approved route of administration for injectable medicines**

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.
For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).

**LOCA: Label — changes as a result of approved corrections made to an entry in the ARTG**

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

**You must submit:**

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.
- For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).

**LOCN: Label — change to names of actives, excipients or dosage forms resulting from changes in the AAN, ingredients database or code tables in TGA eBS**

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

**You must submit:**

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.
- For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).

**LOEI: Label — changes to the method of expressing the content of active ingredients or excipients, in accordance with the current labelling TGO.**

**Conditions**

- The change is minor, such as changing from ‘0.5 mg’ to ‘500 micrograms’.
- There must be no other changes to the label made under this change request.
• The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

• Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

• For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).

**LOPR: Label — changes as a result of product rescheduling (following from changes to the Poisons Standard)**

**Conditions**

• There must be no other changes to the label made under this change request.

• The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

• Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

• For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).

**LOPS: Label — amendments due to implementation of changes that do not require prior notification to the TGA.**

**Conditions**

• Refer [above](#) for the change codes that do not require prior notification to the TGA. There must be no other changes to the label made under this change request.

• The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

• The change can apply to manufacturers who are also product sponsors.

• The change to the address is allowable provided the actual site location does not change.

You must submit:

• Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one
representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

- For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).

**LOSA: Label — amendments resulting from the implementation of a SAR that is either submitted simultaneously or has been previously approved by the TGA**

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.
- For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).

**LOTG: Label — changes to comply with current TGOs for labels that have previously been evaluated and approved by the TGA.**

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.
- For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).
LPCO: Label — addition/deletion of, or change to, the statement of country of origin or manufacture for imported products

Conditions

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.
- The change results from a requirement by other relevant Australian legislation.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

LPDL: Label — changes to the colour, design or layout of labels with no change to content and retaining differentiation of strengths

Conditions

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

LPSP: Label — change to the layout or design of a physician sample pack

Conditions

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.
- May include changes in content if this is to ensure compliance with Australian pharmaceutical industry codes of conduct.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one
representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

**LPWS: Label — addition or deletion of, or change to, the website address of an Australian owned and managed company**

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.
- For addition of, or changes to, a company website address, an assurance that the sponsor has full control over the content of the site.

**LQAB: Label — addition of excipients**

Inclusion of the names of excipients on the medicine label, regardless of whether the substances must be declared on a label to comply with a Ministerial standard.

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

**LQBM: Label — amendment of expression of API content in topical preparations as previously approved**

Amendment to the expression of the proportion of active ingredient in a topical preparation.

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:
Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

**LQHB: Label — addition of 'hypotonic', 'hypertonic' and 'isotonic' for large-volume injections**

Addition of the terms hypotonic, hypertonic and isotonic on the labels of large-volume injections.

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

**LQRB: Label — addition of a previously approved release rate for transdermal patches**

Addition of an approved release rate on the label of medicines that are transdermal patches.

**Conditions**

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.
- For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).
LWAB: Label — addition of a warning or cautionary statement where an incorrect route for method of administration is hazardous

Addition of a warning or cautionary statement to a medicine label, to indicate that an incorrect route or method of administration may be hazardous.

Conditions

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

LWSB: Label — changes to/addition of a warning or precaution statement resulting from an approved safety-related variation to the PI

Change to, or addition of, a warning or cautionary statement on the medicine label, resulting from or relating to a safety-related variation to the entry in the Register for the product made by the Secretary under subsection 9D(2) of the Act, and an associated variation to the Product Information for the product made by the Secretary under subsection 25AA(4) of the Act.

Conditions

- There must be no other changes to the label made under this change request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels and not contravene labelling best practice.

You must submit:

- Copies of the existing labels (with tracked changes) and final copies or mock-ups of the amended labels (for each strength, where applicable) which include any logos, design work or graphics. The copies must be to scale and verify the size/dimensions of the labels and indicate the colours to be used. Where there are multiple pack sizes available, one representative label can be provided (for each strength), as long as the only difference between the labels is the pack size.

- For changes to labels resulting from other regulatory actions that have been either already notified or approved, appropriate evidence of the notification or approval (such as a TGA submission number).

Category 3 requests — Data evaluation required under s. 9D(3)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.
LCDE: Label changes — any changes requiring data for evaluation

Conditions
You must submit:

- Description of the proposed changes.
- Copies of both the currently approved labels and the changed labels. The proposed labels should meet the format requirements of Module 1.3.3 of the CTD format to the stated scale.

Category 3 requests — Data evaluation required under s. 23 (separate and distinct good)

These variations fall under s. 23 of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

DTTR: Trade name replacement
Replacement of trade name.

The AUST R number can be retained

Under s. 16(1) of the Therapeutic Goods Act 1989, a change in trade name means that the renamed product is a separate and distinct good from the existing product, and this requires a new ARTG entry. However, the provisions of the Therapeutic Goods (Groups) Order No. 1 of 2001 allow the AUST R number of the existing product to be retained for the new product, if the new product replaces the existing product.

Conditions

- Only the trade name — not the nonproprietary name of the drug substance — can be changed under this application type.
- The details of the product, including indications and sponsor, should remain the same.

You must submit:

- Proposed replacement trade name.
- The revised label.
- Information on use or non-use of human embryos or human embryonic stem cells, or other material sourced from human embryos or human embryonic stem cells, in the manufacture of the product (this is a requirement under Regulation 9B of the Therapeutic Goods Regulations 1990).
- A clean copy of the PI. Where the proposed change would involve approval of a new PI, a marked-up copy should also be provided.
Pack size changes

Correction to, or completion of, an ARTG entry

Sponsors can request corrections to ARTG entries under s. 9D(1) of the Therapeutic Goods Act 1989. Alternatively, the Secretary can make corrections to ARTG entries under s. 9D(1), at his or her initiative. Refer to the Minor variations to prescription medicines — Process guidance for further information.

CAPS: Pack size & Poison schedule

Conditions

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.

Self-assessable requests (SARs)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

Pack size definitions

For products presented as:

- **discrete dosage units** (for example, tablets, capsules, compressed or moulded suppositories, pessaries, or other single-dose medicine inside a unit container), the pack size is the number of units in the container.

- **non-sterile solid, powder, semi-solid and liquid products**, the pack size is the weight or volume of the container contents.

- **injections** and other **sterile preparations**, the pack size is the number of ampoules, vials, prefilled syringes, bags, bottles and so on per primary pack (carton).

- **transdermal patches**, the pack size is the number of patches per primary pack (carton).

- **pressurised metered-dose preparations** or **dry powder inhalers**, the pack size is the nominal number of doses in the container.

- **non-pressurised metered-dose preparations**, the pack size is the minimum number of doses in the container, or the volume or weight of the container contents.

**Volume of fill** of a sterile product is defined as the nominal volume of solution in the container, the total content of which represents the strength of the product as listed on the label. It may include an overfill.
Inclusion of a new volume of fill, or a change in the existing nominal volume of fill of an injection or a peritoneal dialysis solution is considered under the legislation as a change in product strength and requires a Category 1 application.

**PPRU: Pack size — reduction of number of units in pack size excluding volume of fill of injections or other sterile preparations**

Reducing the number of units (vials, syringes, ampoules, cartridges) in a pack.

**Conditions**

- The change should not be a change in the volume of fill of an injection or other sterile preparation.
- The change should be the result of either of the following:
  - Pharmaceutical Benefits Advisory Committee recommendation (including a larger pack size)
  - to introduce a smaller pack size; or
  - deletion of an existing pack size that is no longer to be supplied.
- The change in pack size should not be accompanied by changes to dosage regimen or indications.
- The label for the new pack size should be the same as for the current pack size, except for quantity of goods or other changes allowed in other sections of this document.
- The additional or changed pack size should be consistent with the treatment recommendations in the PI.
- The container material, size and shape should be either unchanged, or changed in a manner permitted in this document.

You must submit:

- Relevant details regarding the change in pack size.
- A copy of the label for the new pack size, as appropriate.
- Where the proposed change would involve approval of an amended PI, details of changes to the PI.

**Category 3 requests — Data evaluation required under s. 9D(3)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.
PSCA: Packaging — change to or addition of pack size

Change to, or addition of, pack size.

**Conditions**

You must submit:

- Details of the new or additional pack size and the rationale for its introduction.
- Revised labelling, if applicable.
- Where the proposed change requires an update to the PI, details of the amended PI, as outlined in the [Minor variations to prescription medicines — Process guidance](#).
Drug product packaging changes

Correction to, or completion of, an ARTG entry

Sponsors can request corrections to ARTG entries under s. 9D(1) of the *Therapeutic Goods Act 1989*. Alternatively, the Secretary can make corrections to ARTG entries under s. 9D(1), at his or her initiative. Refer to the *Minor variations to prescription medicines — Process guidance* for further information.

CACI: Correct an ARTG entry — Container information

**Conditions**

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.

Notifications

These variations fall under section 9D(2C) of the *Therapeutic Goods Act 1989*.

Conditions that are outlined below the description of each variation type must be met for the request to be processed as a notification.

PPAT: Packaging — introduction of anti-tamper packaging (materials not in contact with drug product)

Introduction of anti-tamper packaging for the drug product.

**Conditions**

- The packaging materials should not be in contact with the product.

You must submit:

- Details of the change.

Category 3 requests — Data evaluation required under s. 9D(3)

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

CCPC: Packaging — changes

Changes to packaging.

This includes container shape, size and material, as well as any measuring or delivery device included in the pack, but excludes container type. It also refers to relevant aspects of packaging of diluents, kits and other product components.
Conditions

- Any change in the material contacting the product will require evidence of biomaterial safety testing and stability data.
- Changes to the container/closure system will require container/closure integrity testing.

You must submit:

- Specifications of the packaging and packaging materials.
- If relevant, biomaterial safety evidence that any new polymeric or rubber packaging materials used that are in contact with the product are free from any leachable toxic impurities and comply with BP/Ph. Eur./USP and Australian requirements for polymeric materials used in packaging of medicines.
- Relevant stability data if the packaging may be expected to be less protective than the currently approved packaging or if the change may affect the stability of the product; otherwise, a commitment to generate such data according to relevant stability guidelines and in accord with GMP requirements. Comparative moisture permeability data of the current and proposed container/closure system may be required.
- If the container/closure system is a child-resistant package or is implied by its presentation to be a child-resistant package, a declaration that the re-closable package meets all of the requirements of the current TGO on child-resistant packaging. State in the declaration which of the recognised international standards on child-resistant packaging the closure complies with, and include evidence of adequate directions for opening and reclosing the package.
- Validation data on the changed measuring/delivery system in the pack.
- For sterile products, sterile manufacture information and sterility testing data, as appropriate, including (for example) validation of aseptic media fills and preservative efficacy test data.
- Revised labelling, instructions for use and any other appropriate information or data that relate to the change, if applicable.
- Where the proposed change would require an update to the PI, details of the amended PI, as outlined in the Minor variations to prescription medicines – Process guidance.

Category 3 requests — Data evaluation required under s. 23 (separate and distinct good)

These variations fall under s. 23 of the Therapeutic Goods Act 1989 and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

PCCT: Packaging — Changes to container type

Minor variations to prescription medicines.

The AUST R number cannot be retained

Under s. 16(1) of the Therapeutic Goods Act 1989, a change in container type means that the repackaged product is a separate and distinct good from the existing product, and this requires a new ARTG entry. The provisions of the Therapeutic Goods (Groups) Order No. 1 of 2001 do not apply so it is not possible for the current AUST R number to be used for the new product.
Conditions

You must submit:

- Description and relevant specifications of container/closure system and materials.
- The proposed shelf life and storage conditions in the new container type.
- Stability data (including physical, chemical and microbiological aspects, as applicable) from at least three production-scale batches, to confirm the stability of the product in the proposed new container. Stability data obtained only from pilot scale batches should be justified.
- Information on use or non-use of human embryos or human embryonic stem cells, or other material sourced from human embryos or human embryonic stem cells, in the manufacture of the product (this is a requirement under Regulation 9B of the Therapeutic Goods Regulations 1990).
- For sterile products, information on sterile manufacture, validation of sterilisation processes, preservative efficacy data and sterility testing data, as appropriate.
- If relevant, biomaterial safety evidence may be required. This is assessed on a case-by-case basis.
- For non-sterile products, details of the revised manufacturing process in the new container, together with process validation data, if appropriate.
- Proposed labels for the product in the new container type.
- A clean copy of the PI. Where the proposed change would involve approval of a new PI, a marked-up copy should also be provided, as outlined in the Minor variations to prescription medicines — Process guidance.
Changes specific to influenza vaccines

Influenza vaccines

Some of the processes for regulating quality-related changes to influenza vaccines are different from the processes for other vaccines. This is because of the changing nature of the vaccine virus strains.

This section may also be applicable to new vaccines that have similar requirements to influenza vaccines.

Self-assessable requests (SARs)

These variations fall under s. 9D(3) of the Therapeutic Goods Act 1989.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

IVMP: Influenza vaccine — strain-specific variations to manufacturing processes

Strain-specific variations to manufacturing processes.

Conditions

- Changes can only be made within previously approved parameters.

You must submit:

- Details of the changes.

IVPL: Influenza vaccine — passage or lot number change of approved reassorted virus or approved virus isolate

Change in the passage or lot number of the approved reassorted virus or approved virus isolate.

Conditions

- The new lot should be derived from an approved reassorted virus or virus isolate, using an approved process.

You must submit:

- The lot number and passage history.

IVRR: Influenza vaccine — reference reagent replacement

Replacement of reference reagent.

Conditions

- Changes can only be made to the reference antigen or antiserum.

You must submit:

- The lot number and source of the reference antigen or antiserum.
IVSL: Influenza vaccine — working seed lot change

Change in the working seed lot.

**Conditions**

- The working seed lot should be derived from an approved reassorted virus or virus isolate, using an approved process.
- Neuraminidase identity should be performed on the first three monovalent pooled harvests from the changed working seed lot, and data should be supplied to the TGA before any lots will be released.

You must submit:

- The lot number and passage history.

**Category 3 requests — Data evaluation required under s. 9D(3)**

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

The changes listed here are representative, rather than exhaustive.

IVSC: Influenza vaccine changes

Changes specific to influenza vaccines.

**Conditions**

The following types of changes that are specific to influenza vaccines require evaluation of data by the TGA:

- change in strain for seasonal influenza vaccines — details of the reassorted virus or virus isolate should be provided in the application.
- Change in the approved reassorted virus or virus isolate for influenza vaccines:
  - this refers to a change in the approved reassorted virus or virus isolate of the same strain used to produce the working seed lot. Details of the approved reassorted virus or virus isolate should be provided in the application.
- Any other changes requiring evaluation, such as strain-specific variations to production processes that exceed approved parameters.

You must submit:

- Description of the proposed change.
- Justification for the proposed change, including changes to test procedures.
- Appropriate validation data.
Other changes

Correction to, or completion of, an ARTG entry

Sponsors can request corrections to ARTG entries under s. 9D(1) of the Therapeutic Goods Act 1989. Alternatively, the Secretary can make corrections to ARTG entries under s. 9D(1), at his or her initiative. Refer to the Minor variations to prescription medicines — Process guidance for further information.

CADF: Correct an ARTG entry — Dosage form

Conditions

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.

CAIC: Correct an ARTG entry — Indications

Conditions

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.

CANC: Correct an ARTG entry — ATC Nordic codes

Conditions

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
- An assurance that the only changes being made to the ARTG entry are those identified in the request.

CAQI: Correct an ARTG entry — Quality-related information, includes labels

Conditions

You must submit:

- Details of the correction or additional information.
- Relevant justification and documentary evidence.
• An assurance that the only changes being made to the ARTG entry are those identified in the request.

**CARA: Correct an ARTG entry — Route of administration**

**Conditions**

You must submit:

• Details of the correction or additional information.
• Relevant justification and documentary evidence.
• An assurance that the only changes being made to the ARTG entry are those identified in the request.

**CASI: Correct an ARTG entry — Sterility information**

**Conditions**

You must submit:

• Details of the correction or additional information.
• Relevant justification and documentary evidence.
• An assurance that the only changes being made to the ARTG entry are those identified in the request.

**CAVI: Correct an ARTG entry — Visual identification / product description**

**Conditions**

You must submit:

• Details of the correction or additional information.
• Relevant justification and documentary evidence.
• An assurance that the only changes being made to the ARTG entry are those identified in the request.

**CAGN: Correct an ARTG entry — Good name**

**Conditions**

You must submit:

• Details of the correction or additional information.
• Relevant justification and documentary evidence.
• An assurance that the only changes being made to the ARTG entry are those identified in the request.
Self-assessable requests (SARs)

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989*.

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable.

OMPS: Medicines and poisons — scheduling changes

<table>
<thead>
<tr>
<th>Changes to medicines and poisons scheduling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any changes to the <em>Standard for the Uniform Scheduling of Medicines and Poisons</em> signal heading and cautionary statements are matters for the states and territories, and therefore should be handled through state and territory authorities.</td>
</tr>
<tr>
<td>If a medicine has been rescheduled from Schedule 4 or 8 to Schedule 2 or 3, any necessary changes to the product should be handled according to the <em>Australian Regulatory Guidelines for Over-the-Counter Medicines</em>, where appropriate.</td>
</tr>
</tbody>
</table>

**Conditions**

- The change in scheduling is from a Schedule 2 or 3 medicine to a Schedule 4 or 8, or from a Schedule 4 to a Schedule 8 medicine.

or

- The medicine has been rescheduled from Schedule 4 or 8 to Schedule 2 or 3, but continues to be regulated as a prescription medicine (see Part 1 of Schedule 10 of the *Therapeutic Goods Regulations 1990*).

You must submit:

- Relevant evidence of the change, such as a copy of the final Advisory Committee on Medicines Scheduling decision.

- A copy of the revised label.

- A clean and marked-up copy of the proposed amended PI, as outlined in the *Minor variations to prescription medicines — Process guidance*. 
Category 3 requests — Data evaluation required under s. 9D(3)

These variations fall under s. 9D(3) of the *Therapeutic Goods Act 1989* and require the submission of data for evaluation.

**OQRC: Quality-related changes (other) that do not create a separate and distinct good**

Changes to other types of quality-related variations where the change does not create a separate and distinct good. For example, a new supplier or manufacturer of albumin for a blood product.

**Conditions**

You must submit:

- Appropriate supporting data for the change(s).
- Where the proposed change would involve approval of an amended PI, details of the amended PI, as outlined in the *Minor variations to prescription medicines — Process guidance*.
- If applicable, and if the change is approved, an updated CPD document.
## Version history

<table>
<thead>
<tr>
<th>Version</th>
<th>Description of change</th>
<th>Author</th>
<th>Effective date</th>
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<tbody>
<tr>
<td>V1.0</td>
<td>Original publication</td>
<td></td>
<td>June 2017</td>
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<tr>
<td>V2.0</td>
<td>Inclusion of notifiable variations to registered medicines. Minor amendments to phrasing and layout.</td>
<td>Scientific Operations Management Section/SEB</td>
<td>December 2017</td>
</tr>
<tr>
<td>V2.1</td>
<td>Minor fixes to typographical errors</td>
<td>Scientific Operations Management Section/SEB</td>
<td>January 2018</td>
</tr>
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