



Australian Government
Department of Health
Therapeutic Goods Administration

Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data

Appendix 1: Variation types – chemical entities

Version 3.1, January 2020

TGA Health Safety
Regulation



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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 before a decision can be made.

This guidance outlines the following types of variations and changes that can be made to [chemically derived](#) (non-biological) prescription medicines currently on the Australian Register of Therapeutic Goods (ARTG) and is split into two parts:

[Part 1: Corrections, notifications and quality information changes](#)

- Changes that do not require prior approval. These are:
 - changes that can be implemented without informing the TGA
 - 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 fee. The applicant must provide legal assurances that all conditions are met and submit supporting data using the approved electronic form.
- Self-assessable requests (SARs) - lower risk variations for which the sponsor can provide an assessment of their own data for the TGA to verify, including to the PI.
- Category 3 requests - variations that require evaluation of quality-related data only. These variation types are intended as representative types, where a summary of the exact changes being requested is included in the cover letter. Includes changes to quality aspects of the PI.

[Part 2: Product information \(PI\) changes](#)

- Minor editorial changes to product information (MEC).
- Safety related requests (SRRs) – requests to either reduce the patient population that can receive the medicine or add a warning or precaution.
- Extension of indications to align with a reference product.

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.

See also:

- [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance.](#)
- For changes to biological medicines see [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Appendix 2: Variation types – biological medicines.](#)

Data supporting variation 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 be required to meet [Good Manufacturing Practice](#).

Refer to each type of variation for full data requirements.

Index of variation types – chemical entities

Variation type	Description	Variation category	Requires update to ARTG data ¹
Part 1: Corrections, notifications and quality information changes			
Active Pharmaceutical Ingredient (API) changes			
	API and intermediate manufacture - alternative site of quality control testing	Does not require reporting to the TGA	
	Ingredients - change to contact details of the local handling agent (including material of biological origin)	Does not require reporting to the TGA	
ACCS	API container - changes to container/closure system of a non-sterile API	Notification	
ACEP	API Certificate of Suitability (CEP) - a revision for a non-sterile API that is not a synthetic polypeptide or prepared by fermentation	Notification	
AMBS	API and intermediate manufacture - change to batch size of a non-sterile API (existing site)	Notification	
AMCS	API site of manufacture - cessation	Notification	Manufacturers
AMIT	API and intermediate manufacture - addition, revision or deletion of in-process control tests and limits	Notification	
AMMC	API and intermediate manufacture - minor manufacturing changes not involving sterilising steps (existing site)	Notification	
AMMF	API starting material/intermediate site of manufacture - change to/addition of (for APIs manufactured by multi-step syntheses or fermentation)	Notification	
AMTA	API site of manufacture - transfer of/addition to an existing manufacturer's site of a non-sterile API that is not prepared by fermentation	Notification	Manufacturers

¹ Also referred to as data within the Provisional ARTG Record (PAR) field

Variation type	Description	Variation category	Requires update to ARTG data ¹
ASAM	API/starting material/intermediate specifications - changes to non-biological test methods for assay and/or residual solvents (including water)	Notification	
ASDR	API re-test period and storage conditions - decrease to re-test period and/or more restrictive storage conditions	Notification	
ASID	API/starting material/intermediate specifications - changes to identification tests	Notification	
ASNL	API/starting material/intermediate specifications - narrowing of limits	Notification	
ASNT	API/starting material/intermediate specifications - addition of new test and limit	Notification	
ASPC	API specifications - changes to physicochemical test methods and limits	Notification	
ASPT	API specifications - amendments resulting from pharmacopoeial or Therapeutic Goods Order (TGO) changes	Notification	
ADSL	Shelf life - Changes to the retest period of the active pharmaceutical ingredient	Category 3	
AMAS	API manufacture - changes to the site(s) of manufacture	Category 3	Manufacturers
AMCM	API manufacture - changes to the synthetic route or the manufacturing process	Category 3	
ASCS	API specifications - changes to the specifications of the active pharmaceutical ingredient, including changes to test methods	Category 3	
Drug product manufacture changes - method, batch size or equipment			
CAMC	Correct an ARTG entry - manufacture	Correction	Manufacturers
DMBS	Drug product manufacture - changes to batch size for products that are not modified release dosage forms	Notification	

Variation type	Description	Variation category	Requires update to ARTG data ¹
DMEL	Drug product manufacture - changes to manufacturing method and/or equipment of semi-solid/liquid dosage forms that are not modified release	Notification	
DMEO	Drug product manufacture - changes to manufacturing method and/or equipment of oral/nasal inhalation dosage forms that are not modified release	Notification	
DMES	Drug product manufacture - changes to manufacturing method and/or equipment for solid dosage forms that are not modified release	Notification	
DMIT	Drug product manufacture - changes to in-process control tests and limits	Notification	
DMRO	Drug product manufacture - reduction or removal of API and excipient overages for ingredients that are not antioxidants or similar	Notification	
DMSE	Drug product manufacture - changes to manufacturing method and/or equipment of sterile dosage forms that are not modified release	Notification	
DMDS	Drug product manufacture - changes to dimensions, shape, inked imprint, embossing or debossing of solid dosage forms	SAR	Visual Identification
DMCM	Drug product manufacture – changes to the method of manufacture	Category 3	
Drug product - site of manufacture changes			
Report separately	Manufacturing - change to manufacturer's name or the manufacturing address, provided the actual site location does not change	Requires reporting to the TGA but not prior approval	
DMDM	Drug product site of manufacture - cessation of a site or deletion of a manufacturing step	Notification	Manufacturers

Variation type	Description	Variation category	Requires update to ARTG data ¹
DMPL	Drug product site of manufacture - change to site of labelling/primary packaging (non-sterile products) or labelling/secondary packaging	Notification	Manufacturers
DMSL	Drug product site of manufacture - change to site of manufacture of non-sterile semi-solid/liquid dosage forms that are not modified release	Notification	Manufacturers
DMSO	Drug product site of manufacture - change to site of manufacture of non-sterile oral/nasal inhalation dosage forms that are not modified release	Notification	Manufacturers
DMSS	Drug product site of manufacture - change to site of manufacture of non-sterile solid dosage forms that are not modified release	Notification	Manufacturers
DMTR	Drug product site of manufacture - change to site performing testing and release for supply	Notification	Manufacturers
DMCS	Drug product site of manufacture - changes to the site(s) of manufacture	Category 3	Manufacturers
Drug product formulation changes			
CAAO	Correct an ARTG entry - animal origin	Correction	Formulation
CAFC	Correct an ARTG entry - formulation	Correction	Formulation
DFCI	Formulation - addition or deletion of, or variation to, an inked imprint	SAR - separate & distinct good	Formulation
DFFC	Formulation - change relating to colouring agent, flavour or fragrance	SAR - separate & distinct good	Formulation
DFCF	Formulation – changes (CE) – Retaining AUST R number	Category 3 - separate & distinct good – Retaining AUST R number	Formulation

Variation type	Description	Variation category	Requires update to ARTG data ¹
DFNA	Formulation – changes (CE) – New AUST R number	Category 3 - separate & distinct good – New AUST R number	Formulation
Drug product specifications or test changes			
DSAM	Drug product specification - changes to non-biological assay method for an active or excipient that is not a radiopharmaceutical	Notification	
DSID	Drug product specification - changes to identification tests for the active or excipient	Notification	
DSIP	Drug product specification - changes from an in-house test method to a pharmacopoeial test method	Notification	
DSNL	Drug product specification - narrowing of test limits	Notification	
DSNT	Drug product specification - addition of test and limit	Notification	
DSPL	Drug product specification - minor changes to physicochemical test methods and limits	Notification	
DSPT	Drug product specification - changes resulting from pharmacopoeial or TGO requirements	Notification	
DSST	Drug product specification - changes to sterility test method	Notification	
DSCS	Drug product specifications - changes to specifications, including changes to test methods	Category 3	
Excipients changes			
	Excipients (not of animal or human origin) - changes to the manufacturing process and/or site (same specifications)	Does not require reporting to the TGA	

Variation type	Description	Variation category	Requires update to ARTG data ¹
EMRS	Excipient manufacture (from Category IC ruminant tissues) - changes in source (from animal to non-animal) and/or manufacturing process or site	Notification	Formulation
ESAM	Excipient specification - change to assay method	Notification	
ESIP	Excipient specification - change from an in-house to a pharmacopoeial test method	Notification	
ESNL	Excipient specification - narrowing of limit	Notification	
ESNT	Excipient specification - new test and limit	Notification	
ESPT	Excipient specification - changes resulting from pharmacopoeial or TGO requirements	Notification	
ESCS	Excipient specification - changes to the specifications of the excipients, raw materials and starting materials	Category 3	
EMPC	Excipients of animal origin - change to source	Category 3	Formulation
EMPM	Excipients of animal origin - change to method of manufacture	Category 3	
Container/closure system changes			
	Non-sterile container - changes to the supplier or manufacturer if same material and specifications	Does not require reporting to the TGA	
CACI	Correct an ARTG entry - container information	Correction	Container & Shelf Life
CCCA	Container/closure - change to components	Notification	
CCSS	Container/closure - change to size and shape for non-sterile dosage forms	Notification	
CCST	Container/closure - changes to specification and test methods	Notification	

Variation type	Description	Variation category	Requires update to ARTG data ¹
CMDT	Container/closure material - decrease in thickness for blister packs, strip packs and sachets for non-sterile solid or semi-solid dosage forms	Notification	
CMIT	Container/closure material - increase in thickness for non-sterile solid, semi-solid, semi-liquid or liquid dosage forms	Notification	
CMBP	Container/closure material - changes to material used for blister packs, strip packs and sachets of non-sterile dosage forms	SAR	Container & Shelf Life
CMBT	Container/closure material - changes to material used for bottles, jars and tubes of non-sterile dosage forms	SAR	Container & Shelf Life
CCSC	Container/closure system - changes to container components and/or dimensions	Category 3	Container & Shelf Life
PCCT	Packaging - changes to container type – New AUST R number	Category 3 - separate & distinct good – New AUST R number	Container & Shelf Life
Pack size changes			
CAPS	Correct an ARTG entry - pack size & poison schedule	Correction	Pack Size & Poison Schedule
PSAC	Pack size - addition or change to pack size excluding volume of fill of injections or other sterile preparations	SAR	Pack Size & Poison Schedule
PSCA	Pack size - change to, or addition of, pack size	Category 3	Pack Size & Poison Schedule
Product shelf life or storage conditions changes			
CASL	Correct an ARTG entry - shelf life / storage condition	Correction	Container & Shelf Life
DSL D	Shelf life - decrease and/or more restrictive storage conditions	SAR	Container & Shelf Life

Variation type	Description	Variation category	Requires update to ARTG data ¹
DSLE	Shelf life - extension according to an approved stability-testing protocol	SAR	Container & Shelf Life
DSLCL	Shelf life - changes to the shelf life or storage conditions of the drug product.	Category 3	Container & Shelf Life
Product information (PI) changes: Quality aspects, corrections and self-assessable requests (SARs)			
CAPI	Correct an ARTG entry – Product Information (PI)	Correction	
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	
PISR	PI - putting into effect the guidelines in section 20.2 of Guidance 20: Radiopharmaceuticals	SAR	
PICC	PI - changes to quality aspects of the product information	Category 3	
Product label changes			
	Changes to labels that do not require reporting to the TGA.	Does not require reporting to the TGA	

Variation type	Description	Variation category	Requires update to ARTG data ¹
LOCI	Label - consequential change resulting from a change approved under subsection 9D(3) or conditions imposed under subsection 28(3)	Notification	
LPCL	Label - addition or deletion of, or change to, the company logo or livery	Notification	
LPCP	Label - addition or deletion of, or change to, the pictogram of a product or its dosage form	Notification	
LPCS	Label - addition or deletion of, or change to, the name or address of the Australian sponsor or supplier of the product	Notification	
LPDG	Label - deletion of existing graphics, pictures or diagrams, and any associated text	Notification	
LPDR	Label - deletion of repeated text (present elsewhere on a label) from selected side panels provided that the information is not mandatory	Notification	
LPIA	Label - addition of simple instructional/informational/anti-tampering statements, or information about a changed appearance of the dosage form	Notification	
LPOP	Label - addition or deletion of, or change to, label text of outer protective pouches or overwraps of the container or primary pack	Notification	
LPPS	Label - adding information either on label or as insert advising of patient support program (PSP)	Notification	
LPQR	Label - inclusion of QR code	Notification	
LPRP	Label - removal of phrases such as 'New formulation', 'New appearance' after a period of time.	Notification	
LQAE	Label - addition of excipients	Notification	
LQAT	Label - amendment of expression of API content in topical preparations as previously approved	Notification	

Variation type	Description	Variation category	Requires update to ARTG data ¹
LQHI	Label - addition of 'hypotonic', 'hypertonic' and 'isotonic' for large-volume injections	Notification	
LQRT	Label - addition of a previously approved release rate for transdermal patches	Notification	
LWAH	Label - addition of a warning or cautionary statement where an incorrect route for method of administration is hazardous	Notification	
LWSR	Label - changes to/addition of a warning or precaution statement resulting from an approved safety-related variation to the PI	Notification	
LOAI	Label - addition of a new TGA-approved route of administration for injectable medicines	SAR	
LOCA	Label - changes as a result of approved corrections made to an entry in the ARTG	SAR	
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	SAR	
LOEI	Label - changes to the method of expressing the content of active ingredients or excipients, in accordance with the current labelling TGO	SAR	
LOPR	Label - changes as a result of product rescheduling (following from changes to the Poisons Standard)	SAR	
LOPS	Label - amendments due to implementation of changes that do not require prior approval from the TGA	SAR	
LOSA	Label - amendments resulting from the implementation of a SAR that is either submitted simultaneously or has been previously approved by the TGA	SAR	
LOTG	Label - changes to comply with current TGOs for labels that have previously been evaluated and approved by the TGA	SAR	

Variation type	Description	Variation category	Requires update to ARTG data ¹
LPCO	Label - addition/deletion of, or change to, the statement of country of origin or manufacture for imported products	SAR	
LPDL	Label - changes to the colour, design or layout of labels with no change to content and retaining differentiation of strengths	SAR	
LPSP	Label - change to the layout or design of a physician sample pack	SAR	
LPWS	Label - addition or deletion of, or change to, the website address of an Australian owned and managed company	SAR	
LCDE	Label changes - any changes requiring evaluation	Category 3	
DTTR	Trade name replacement – Retaining AUST R number	Category 3 - separate & distinct good – Retaining AUST R number	Good Name
Other changes			
CADF	Correct an ARTG entry - dosage form	Correction	Dosage Form
CAGN	Correct an ARTG entry - good name	Correction	Good Name
CAIC	Correct an ARTG entry - indications	Correction	Indications
CANC	Correct an ARTG entry - ATC Nordic codes	Correction	ATC Nordic Codes
CAQI	Correct an ARTG entry - quality-related information, includes labels	Correction	
CARA	Correct an ARTG entry - route of administration	Correction	Route of Administration
CASI	Correct an ARTG entry - sterility information	Correction	Sterility Information
CAVI	Correct an ARTG entry - visual identification / product description	Correction	Visual Identification

Variation type	Description	Variation category	Requires update to ARTG data ¹
OCPS	Medicines and poisons - change in scheduling	SAR	Pack Size & Poison Schedule
SARO	Other self-assessable changes - an application using this type must include written advice from the TGA	SAR	
OCQD	Other quality changes that do not create a separate and distinct good	Category 3	
Associated changes (to be used when one variation requires multiple PAR fields to be updated)			
Changes associated with formulation changes - DFCI and DFFC			
ZFSM	ARTG data - Manufacturer changes associated with DFCI or DFFC	SAR	Manufacturers
ZFSV	ARTG data - Visual identification changes associated with DFCI or DFFC	SAR	Visual Identification
Changes associated with formulation change - DFCF or new name - DTTR			
ZFRC	ARTG data - Container and shelf life changes associated with DFCF/PFCF or DTTR - Retaining AUST R number	Category 3 - separate & distinct good - Retaining AUST R number	Container & Shelf Life
ZFRM	ARTG data - Manufacturer changes associated with DFCF/PFCF or DTTR - Retaining AUST R number	Category 3 - separate & distinct good - Retaining AUST R number	Manufacturers
ZFRN	ARTG data - Good name changes associated with DFCF/PFCF - Retaining AUST R number	Category 3 - separate & distinct good - Retaining AUST R number	Good Name

Variation type	Description	Variation category	Requires update to ARTG data ¹
ZFRO	Other consequential changes to the dossier associated with DFCF/PFCF or DTTR - Retaining AUST R number	Category 3 - separate & distinct good - Retaining AUST R number	
ZFRP	ARTG data - Pack size and poison schedule changes associated with DFCF/PFCF or DTTR - Retaining AUST R number	Category 3 - separate & distinct good - Retaining AUST R number	Pack Size & Poison Schedule
ZFRS	ARTG data - Sterility changes associated with DFCF/PFCF or DTTR - Retaining AUST R number	Category 3 - separate & distinct good - Retaining AUST R number	Sterility Information
ZFRV	ARTG data - Visual identification changes associated with DFCF/PFCF or DTTR - Retaining AUST R number	Category 3 - separate & distinct good - Retaining AUST R number	Visual Identification
Changes associated with formulation change - DFNA or packaging change - PCCT			
ZFNC	ARTG data - Container and shelf life changes associated with DFNA/PFNA - For the new AUST R number	Category 3 - separate & distinct good - New AUST R number	Container & Shelf Life
ZFNM	ARTG data - Manufacturer changes associated with DFNA/PFNA or PCCT - For the new AUST R number	Category 3 - separate & distinct good - New AUST R number	Manufacturers

Variation type	Description	Variation category	Requires update to ARTG data ¹
ZFNN	ARTG data - Good name changes associated with DFNA/PFNA or PCCT - For the new AUST R number	Category 3 - separate & distinct good - New AUST R number	Good Name
ZFNO	Other consequential changes to the dossier associated with DFNA/PFNA or PCCT - For the new AUST R number	Category 3 - separate & distinct good - New AUST R number	
ZFNP	ARTG data - Pack size and poison schedule changes associated with DFNA/PFNA or PCCT - For the new AUST R number	Category 3 - separate & distinct good - New AUST R number	Pack Size & Poison Schedule
ZFNS	ARTG data - Sterility changes associated with DFNA/PFNA or PCCT - For the new AUST R number	Category 3 - separate & distinct good - New AUST R number	Sterility Information
ZFNV	ARTG data - Visual identification changes associated with DFNA/PFNA or PCCT - For the new AUST R number	Category 3 - separate & distinct good - New AUST R number	Visual Identification
Part 2: Product information (PI) changes			
Product information (PI) changes: Minor editorial changes and safety related requests (SRRs)			
PIME	PI - make minor editorial changes	MEC	
PIID	PI - remove an indication with data	SRR	Indications
PIIN	PI - remove an indication - no data	SRR	Indications
PIOD	PI - make safety related changes with data	SRR	

Variation type	Description	Variation category	Requires update to ARTG data ¹
PION	PI - make safety related changes no data	SRR	
Extension of indications to align with a reference product			
PIES	Extension of specific indications to align with a reference product	Extension of indications to align with a reference product	Indications
Associated changes to PI (to be used when one variation requires multiple PAR fields to be updated)			
Changes associated with extension of indications - PIES			
PIEP	Additional pack sizes resulting from extension of indications to align with a reference product	Extension of indications to align with a reference product	Pack Size & Poison Schedule

1. Corrections, notifications and quality information changes

The Variation e-form for prescription medicines has four category groups which are described in [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#):

- Correct an ARTG entry
- Notification
- Quality information
- Product information (PI).

Part 1 of this guidance describes the changes that can be made within the corrections, notifications and quality information category groups. This includes changes to the quality aspects of the PI, corrections to the PI and self-assessable requests (SARs) related to PI information.

For changes that can be made within the product information (PI) category including minor editorial changes, safety related requests and extension of indications to align with a reference product see [Part 2: Product information \(PI\) changes](#).

1.1 Active Pharmaceutical Ingredient (API) changes

1.1.1 Changes that do not require reporting to the TGA

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

API and intermediate manufacture - alternative site of quality control testing

You do not need to inform the TGA if you are making a variation to the quality control testing site of the API or intermediate in API manufacture.

Module 3 should be updated to reflect the new alternative site when the next variation is submitted to the TGA. Refer to [Evidence of GMP compliance for prescription medicines](#) for information about when you are required to provide evidence of GMP.

Conditions

- The new site must be GMP compliant.
- There must not be any changes to the existing test methods used for testing the API.

Data requirements

- You must generate appropriate technology transfer data of the approved test methods to the proposed site.

Ingredients - change to local handling agent contact details (including material of biological origin)

You do not need to inform the TGA if you are making a variation that changes the contact details of the local handling agent for the API and excipient. This includes material of biological origin.

Conditions

- Same site and method of manufacture, specifications and, where applicable, biological source, including geographical origin and supplier.

1.1.2 Notifications

These variations fall under s. 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.

ACCS: API container - changes to container/closure system of a non-sterile API

Changes to the container or closure system used to store a non-sterile API.

Conditions

- The API must not be sterile.
- The material of the container/closure must be either unchanged or is changed to a more protective material.
- The thickness of the material must be either unchanged or increased.
- There must either be no change in retest period/storage conditions, or a decrease in retest period and/or more stringent storage conditions are applied in the new container/closure system.

Data requirements

You must submit:

- Details of the new container/closure system.
- Details of the new retest period or storage conditions, if changed.

You must generate the following:

- Relevant comparative moisture permeability data for the current and proposed material demonstrating either equivalent or better moisture protection.
- Initial stability testing data of the API in the new container/closure system conducted in accordance with relevant stability testing guidelines.

ACEP: API Certificate of Suitability (CEP) - a revision for a non-sterile API that is not a synthetic polypeptide or prepared by fermentation

This covers all changes to the data package of the API that have been reviewed by the European Directorate for the Quality of Medicines and Healthcare (EDQM) where the EDQM subsequently issued a revised Certificate of Suitability (CEP), or have declared that a revised CEP is not required.

Conditions

- The API must not be manufactured wholly or substantially by fermentation.
- The API must not be a synthetic polypeptide.
- The API must not be manufactured as a sterile drug substance.
- The current CEP must have been approved previously by the TGA.
- The revised CEP must be the next issued version from that approved by the TGA. Additional consecutive updates can only be included:
 - they follow the 5-year renewal (with no other changes) and/or
 - the changes are for minor administrative updates and/or
 - the drug substance has not been used to manufacture any drug products supplied in Australia.
- Where changes to the API specification are involved (including test parameters, limits and test methods), the same changes must be adopted by the product sponsor and/or drug product manufacturer, and any new test methods must be validated as suitable for use.
- Where the change to the CEP is a change to the site of API manufacture, the site must have either:
 - a licence to manufacture the API (if the site is in Australia) or
 - sponsor-specific GMP clearance (if the site is overseas) that is valid at the time of the application.

Data requirements

You must submit:

- Documentary evidence that the current CEP has been previously approved by the TGA.
- The updated CEP, including any annexes, or a declaration from the EDQM that, due to the nature of the changes, an updated CEP was not issued.
- A summary of the changes made to the API that resulted in the revision of the CEP.
- A declaration that any test requirements in addition to those in the CEP that were previously approved by the TGA will continue to apply.
- A declaration that no significant changes to the API have been made since the revised CEP was issued.
- The revised API specification, including test methods, adopted by the API manufacturer and the drug product manufacturer/product sponsor (as relevant).



A GMP clearance or manufacturing licence is **not** required for the manufacturing site of intermediates or the site of milling/micronisation of the final drug substance. If, however, the milling of the final API occurs in Australia the site will require a GMP licence.

If a manufacturing site for an intermediate is included in the CEP, please make this clear to avoid confusion about the actual site of manufacture of the API. Refer to [Evidence of GMP compliance for prescription medicines](#) for information about when you are required to provide evidence of GMP.

You must generate the following data:

- Relevant comparative data for pre-change and post-change batches of the API (if the revision to the CEP is due to changes to the method of synthesis that involve using different crystallisation solvents, a different purification process, or micronisation of the final drug substance).
- Comparative data using validated test methods to show that:
 - there is no change in the crystalline (polymorphic) form of the final substance (if relevant) and
 - the particle size distribution profiles (tested by a laser diffraction or other equivalent method) remain comparable and within the same ranges as the pre-change API. Alternatively comparative dissolution profiles must be generated.
- Comparative batch data from at least one production-scale batch of the final drug substance manufactured or tested according to the changed process, which demonstrate compliance with any revised API specification.

AMBS: API and intermediate manufacture - change to batch size of a non-sterile API (existing site)

Change to the size of a manufacturing batch of a non-sterile API or its intermediates.

Conditions

- Any increase in batch size must be less than 10 fold from that last evaluated by the TGA.
- There must be no change in route of synthesis (including solvents used in the final purification of the API), other than any necessary adjustment to processing conditions or use of different equipment.
- The change must not be due to unexpected events arising during manufacture or to stability concerns.
- The API must not be a sterile substance.

Data requirements

You must submit:

- Details of the new manufacturing batch size.

You must generate the following data:

- Comparative batch data demonstrating there is no significant difference in the tested parameters, particularly particle size distribution, polymorphism and impurity profiles.

AMCS: API site of manufacture - cessation

Cessation of an approved site for the manufacture of the API.

Requires update to ARTG data: Manufacturers

Conditions

- There must be at least one other registered site of manufacture for the API.



A GMP clearance or manufacturing licence is required for the principal manufacturing site of the final drug substance. Exceptions are some common inorganic salts and simple organic compounds. For more information see guidance on [drug master files](#) (active substance master files).

Data requirements

You must submit:

- The name and address of the manufacturer to be ceased.
- A current [TGA Business Services](#) printout for the product or a copy of the TGA approval showing that at least one registered site of manufacture of the API remains to perform the relevant steps of manufacture.

AMIT: API and intermediate manufacture - addition, revision or deletion of in-process control tests and limits

Addition, revision or deletion of in-process control tests and associated limits applied during manufacture of the API or its intermediates.

Conditions

- The change must be consistent with any applicable principles of the [Guide to Good Manufacturing Practice for Medicinal Products](#).
- The change must not be due to adverse events during manufacture.
- The change must result in equivalent or improved quality of the final isolated material.
- The specifications of the API and/or intermediates may only be changed in ways permitted in other parts of this guidance document or remain unchanged.
- The new test method must not be a biological method.

Data requirements

You must submit:

- Details of the new in-process control tests and limits.

You must generate the following data:

- Appropriate validation data for the in-process control test method.
- Batch analytical data from testing of three batches using the current and proposed methods demonstrating the results are within the same ranges.

AMMC: API/starting material/intermediate manufacture - minor manufacturing changes not involving sterilising steps (existing site)

Minor changes to the manufacture of the API, starting material or intermediates (i.e. equipment or process changes to improve efficiency), excluding changes to sterilising steps.

Conditions

- The change must be consistent with any applicable principles of the [Guide to Good Manufacturing Practice for Medicinal Products](#).
- The synthetic route must remain the same, and no new reagents, solvents or catalysts are to be used in the amended process.
- The change must not involve any sterilising steps.
- The specifications of the API, starting materials and intermediates may only be changed in ways permitted in other parts of this document or remain unchanged.

Data requirements

You must submit:

- Details of the amended manufacturing process, including the synthesis flowchart.

You must generate the following data:

- Comparative batch data for the API/starting material/intermediate demonstrating there are no significant differences in the purity profiles or physicochemical properties.

AMMF: API starting material/intermediate site of manufacture - change to/addition of (for APIs manufactured by multi-step syntheses or fermentation)

Transfer to, or addition of, an alternative site for the manufacture of intermediates for APIs that are manufactured by multi-step synthesis, which may include intermediates prepared wholly or partially by fermentation.

Conditions

- The intermediates must be isolated chemical species and be at least three steps back in the synthetic scheme from the API (purification procedures do not count as steps of synthesis).
- The synthetic route must remain the same, and no new reagents, solvents or catalysts are to be used at the new site.
- The specification limits of starting materials or intermediates must be the same or tighter.
- For intermediates prepared wholly or partially by fermentation:
 - there must be either no change in the strain of the producer organism used or, where there is a change, details of the new producer organism must be provided and the component profiles of the final fermentation broth at harvest made from the new and old strain must be the same.
 - there must be no changes to the scale of operation of the fermentation tank and fermentation processes.
 - there must be no changes to the nature of the media ingredients, particularly precursors, activators or components of biological or animal origin (although changes to the quantities used are acceptable, provided that they are not a result of a change in scale of operation).

Data requirements

You must submit:

- The name and site address of the new manufacturer(s) of the starting material(s) or intermediate(s).
- The route of synthesis of the API.
- The name or code number of the intermediates for which the alternative site of manufacture is sought.

You must generate the following data:

- Comparative batch data (including impurity levels) for the starting material(s) or intermediate(s) manufactured at the current and proposed sites using validated test methods demonstrating that there are no significant differences in purity profiles.
- Comparative batch data for API synthesised using starting material(s) or intermediate(s) from the current and proposed sites demonstrating that there are no significant differences in purity profiles.

AMTA: API site of manufacture - transfer of/addition to an existing manufacturer's site of a non-sterile API that is not prepared by fermentation

Transfer to, or addition of, an alternative site of manufacture of non-sterile APIs that are not prepared by fermentation, but by chemical synthesis or through isolation from a natural source as pure chemical entities.

Requires update to ARTG data: Manufacturers

Conditions

- The API must be prepared by chemical synthesis or isolated from a natural source as pure chemical entities.
- The API must not be prepared wholly or partially by fermentation, and must not be sterile.
- There must be no change to the existing method of synthesis, including to any intermediates and any solvents or reagents used in the synthesis and purification of the drug substance (the API), or any other aspect of manufacture and specifications.



This change only applies where the sponsor of the drug product or the new API manufacturer knows the **full route of synthesis and all other details of manufacture** of the API at both sites.

- The manufacturing batch size remains unchanged or smaller.
- The new site must either have:
 - a current manufacturing licence issued by the TGA (Australian manufacturers) for this type of manufacture or
 - a sponsor-specific GMP clearance (if the site is overseas) that is valid at the time of the application for this type of manufacture.

Data requirements

You must submit:

- The name and address of the new manufacturing site and GMP clearance number.
- The flowchart of the route of synthesis at the existing site and the new site of manufacture.
- The manufacturing batch size at the new site.

You must generate the following data:

- Comparative batch data for three batches of the API from the proposed site. This data must demonstrate that all results (including impurity profiles, particle size distribution and polymorphic forms) are either:
 - within the same range as three batches manufactured at the current site (that is, no new impurities or polymorphic forms are present) or
 - remain unchanged.

ASAM: API/starting material/intermediate specifications - changes to non-biological test methods for assay and/or residual solvents (including water)

Changes to a non-biological method used for assaying or residual solvent testing (including testing for water where this may be present) of the API, starting materials for API synthesis or intermediates created in the synthetic process.

Conditions

- The proposed method must not be a biological method.
- Validation data from the proposed method must demonstrate either:
 - an improvement in at least one of precision, accuracy or specificity, without a reduction in the other parameters or
 - an improvement in specificity or accuracy with reduced precision (provided precision remains within the specified limits).

Data requirements

You must submit:

- A summary description of the change and details of the new method.

You must generate the following data:

- Validation data for the proposed method.
- Data for three batches of the API tested using the current and proposed methods demonstrating equivalency of both methods.

ASDR: API re-test period and storage conditions - decrease to re-test period and/or more restrictive storage conditions

Decrease in the re-test period, or application of more restrictive storage conditions, for APIs.

Conditions

- The change should not be the result of unexpected events arising during manufacture or because of stability concerns.

Data requirements

You must submit:

- Reasons for the change.
- Details of the new retest period and/or storage conditions.
- An assurance that you possess adequate stability data for at least three production-scale batches of the API to support the new retest period and/or storage conditions.

ASID: API/starting material/intermediate specifications - changes to identification tests

Changes to identification tests used for the API, starting materials for API synthesis or intermediates created in the synthetic process.

Conditions

- The changes to identification tests must:
 - be from a less specific to a more specific identification test (for example, from an ultraviolet/visible spectrophotometric or chromatographic method, such as thin layer chromatography, gas chromatography or high-performance liquid chromatography (HPLC), to a conventional infrared spectroscopic method) and/or
 - vary the existing identification test (for example, an HPLC test that has been shown to improve or at least maintain the specificity of the method) and/or
 - replace an existing identification test with a near infrared spectroscopic identification test and/or
 - include a new identification test in addition to an existing identification test.
- Any additional identification test must not serve as an alternative identification test.
- For near infrared spectroscopy tests, the method development and other data requirements (including data collection, establishment of the spectral reference library, calibration and validation of the method) must comply with the [currently adopted European Medicines Agency \(EMA\) guideline](#) on the use of near-infrared spectroscopy.

Data requirements

You must submit:

- The revised set of specifications.
- Details of the identification test method.

ASNL: API/starting material/intermediate specifications - narrowing of limits

Any revision of the specifications for testing of the API, starting materials for API synthesis or intermediates created in the synthetic process must make the limits applied to the test results more stringent.

Conditions

- The proposed limits must be consistent with any applicable official standard or adopted guidelines.

- The grade of material must not change (for example, unmicronised to micronised material).

Data requirements

You must submit:

- The revised set of specifications for the starting materials, intermediates or API (as applicable).

You must generate the following data:

- Data for at least three production-scale batches demonstrating compliance with the proposed test and limits.

ASNT: API/starting material/intermediate specifications - addition of new test and limit

Addition of a new test and associated limits to the approved specifications for the API, starting materials for API synthesis or intermediates created in the synthetic process.

Conditions

- The change must not result from an altered method of manufacture that changes the material's quality characteristics (such as micronisation).
- The proposed method must be validated.
- Applied limits must be based on batch analytical data, and comply with any applicable official standard or adopted guidelines.
- The change must not involve a genotoxic impurity.

Data requirements

You must submit:

- Details of the new method.
- The revised set of specifications for the starting materials, intermediates or API (as applicable).

You must generate the following data:

- Comparative batch data for at least three commercial batches demonstrating compliance with the proposed test and limit.

ASPC: API specifications - changes to physicochemical test methods and limits



Physicochemical parameters include pH, hardness, friability, colour, particle size distribution, particulate matter contamination, density, specific gravity, optical rotation, extractable volume, osmolality, osmolarity and viscosity.

Conditions

- The test limit must either remain unchanged or be more stringent.
- The amended method must have been validated or deemed comparable.
- The test principle must remain unchanged.

Data requirements

You must submit:

- Details of the new method together with a summary description of the change.

You must generate the following data:

- Appropriate validation data or comparison data for the new method.

ASPT: API specifications - amendments resulting from pharmacopoeial or TGO changes

Changes to the specifications for the API as a result of amendments to requirements in a default standard (i.e. a monograph in the British pharmacopoeia [BP], The United States Pharmacopoeia and The National Formulary [USP-NF] or the European Pharmacopoeia [EP]) or relevant requirements in an applicable standard made by the Minister under section 10 of the [Act](#).

Conditions

- The API must already be tested to the existing pharmacopoeial or Therapeutic Goods Order (TGO) requirements.
- The requirements applied from one pharmacopoeia must not be changed to another (e.g. changing from the BP to the USP requires the submission of data for evaluation).
- The new pharmacopoeial monograph or amended TGO must be applicable to the API.
- Any tests that were performed in addition to those of the pharmacopoeial monograph must continue to be applied, except where the test was required by the old monograph and not by the new one.

Data requirements

You must submit:

- The revised set of specifications for the API.

1.1.3 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.

ADSL: Shelf life - Changes to the retest period of the active pharmaceutical ingredient

Any proposed changes to the retest period of an API can be submitted as part of this Category 3 variation type.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- Stability data generated according to International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines on at least three production-scale batches of the API to support the change. Data from fewer batches or pilot-scale batches may be acceptable, if justified.

AMAS: API manufacture - changes to the site(s) of manufacture

Any proposed changes to the site of manufacture of an API can be submitted as part of this Category 3 variation type.

Requires update to ARTG data: Manufacturers

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- GMP evidence for the new site (that is, the Australian manufacturing licence for an Australian site or a current GMP clearance letter for an overseas site). The Australian licence or GMP clearance letter should cover the relevant manufacturing steps and should be valid (before expiry) at the time of application.
- Process validation data, including full details of the method of synthesis and relevant flow diagrams, and validation of sterile manufacture and sterile processes, if applicable.
- If the API exhibits polymorphism, relevant data to demonstrate that the approved polymorphic form is produced.
- Comparative impurity profile data from representative batches from current and new sites of manufacture, using a validated test method.
- Comparative particle size distribution data from at least three batches of pre-variation API and at least one batch of post-variation API to demonstrate comparability in particle size profile.
- Validation data that demonstrate the suitability of the API from the new site for use in the dosage form for which it is intended (for example, comparative dissolution profiles for solid dosage forms, drug mass aerodynamic particle size distribution for inhalation products) or justification for not providing such data. Where multi-strength (more than two) products are involved, comparative data for the highest and lowest strengths should suffice if the various strengths are direct scale or their formulations are closely similar.
- A Drug Master File (DMF) with accompanying letter of access, a CEP with accompanying letter of access, or a declaration that the manufacturing process and quality control are the same as those used at the currently approved manufacturing sites, or a description of any differences between the processes at the different sites (refer to [Guidance 11: Drug Master Files and Certificates of Suitability of a Monograph of the European Pharmacopoeia for drug substances](#) for further details).
- Certificates of analysis for at least three production-scale batches manufactured at the new site that demonstrate the manufacturer's ability to produce material that meets the currently approved specifications, including particle size limits and polymorphic form.

AMCM: API manufacture - changes to the synthetic route or the manufacturing process

Any proposed changes to the synthetic route or manufacturing process can be submitted as part of this Category 3 variation type. For example, increases in batch size, changes to manufacture of key intermediates or redefining a starting material.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- A description (including flow diagram) of the changed manufacturing process, including any changes to manufacturing batch size and in-process controls.
- If redefining a starting material, justification for the choice of the starting material. Provide the pre-starting material synthetic process and details of controls of starting material impurities, including metal catalysts and residual solvents.
- Validation of the process.
- If the API 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 assurance regarding self-assessment of TSE risks of such materials (see variation type [EMRS](#))
- A description and discussion of any resulting changes in impurities.
- Comparative impurity profile data from three batches of pre-variation material and at least one production batch of post-variation material using a validated test method.
- Comparative particle size distribution data from at least three batches of pre-variation and at least one batch of post-variation API to demonstrate comparability in particle size profile.
- Certificates of analysis for at least one production batch of API manufactured using the new process that demonstrates the manufacturer's ability to meet the currently approved specifications, including polymorphic form and particle size distribution (using laser diffraction method), if appropriate. An assurance that certificates of analysis for another two batches showing compliance with the currently approved API specifications will be generated should also be provided.
- An updated Drug Master File (DMF) or Certificate of Suitability (CEP) (refer to [Guidance 11: Drug Master Files and Certificates of Suitability of a Monograph of the European Pharmacopoeia for drug substances](#) for further details), if relevant.
- Where a change is to late stages of synthesis, crystallisation, purification or milling, either relevant comparative data of the dosage form (for example, dissolution, drug mass, aerodynamic particle size distribution) manufactured from at least three batches of pre-variation and at least one batch of post-variation API, or a cogent justification for not providing such data.
- Stability data for post-variation API in accordance with the relevant adopted EMA/ICH guidelines, or a statement of commitment to carry out such studies to verify any applied retest period of the API. Refer to [ARGPM Guidance on Stability testing for prescription medicines](#) for further details. Additional accelerated and long-term stability data for the drug product using the post-variation API may be necessary, in accordance with EMA guidelines.

ASCS: API specifications - changes to the specifications of the active pharmaceutical ingredient, including changes to test methods

Any proposed changes to the specifications of the API can be submitted as part of this Category 3 variation type.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- A copy of the revised specification. This should be consolidated to apply to all sites of API manufacture, where relevant.
- Justification for the proposed changes, including changes to test methods.
- Validation of any changed test methods. Method cross-validation data against alternative or pharmacopoeial methods may also be required, if relevant.
- Certificates of analysis for at least three representative production-scale batches of the bulk API that demonstrate the stability of the API.

1.2 Drug product manufacture changes - method, batch size or equipment

These changes may be made to any products containing chemical entities (including sterile products) covered by this document except those that are specifically excluded under each change type.

1.2.1 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 [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#) for further information.

CAMC: Correct an ARTG entry – Manufacturer

Requires update to ARTG data: Manufacturers

Conditions

- Data is submitted as described below.

Data requirements

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.

1.2.2 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.

DMBS: Drug product manufacture - changes to batch size for products that are not modified release dosage forms

Changes to the size of the manufacturing batch of drug products, where these are not modified release dosage forms.

Conditions

- The change must not be an increase in batch size for sterile products or products manufactured under sterile conditions.
- For sterile products, a decrease in manufacturing batch size must be either:
 - not accompanied by any change in sterile manufacturing process or
 - where there has been a change in sterile manufacturing process, the specific conditions in [DMSE: Drug product manufacture - changes to manufacturing method and/or equipment of sterile dosage forms that are not modified release](#) have been met.
- The product must not be a modified-release dosage form. This includes enteric-coated tablets, enteric capsules and transdermal patches.
- The new manufacturing batch size must be validated in accordance with applicable principles of the [Guide to Good Manufacturing Practice for Medicinal Products and any relevant guidelines adopted by the TGA](#).

Data requirements

You must submit:

- Details of the new manufacturing batch size, with the revised batch manufacturing formula.

You must generate the following data:

- Additional validation data as required for the dosage form, as appropriate:
 - For solid dosage forms, see [DMES: Drug product manufacture - changes to manufacturing method and/or equipment of solid dosage forms that are not modified release](#).
 - For semi-solid/liquid dosage forms, see [DMEL: Drug product manufacture - changes to manufacturing method and/or equipment of semi-solid/liquid dosage forms that are not modified release](#).
 - For oral/nasal inhalation dosage forms, see [DMEO: Drug product manufacture - changes to manufacturing method and/or equipment of oral/nasal inhalation dosage forms that are not modified release](#).
 - For sterile dosage forms, see [DMSE: Drug product manufacture - changes to manufacturing method and/or equipment of sterile dosage forms that are not modified release](#).

DMEL: Drug product manufacture - changes to manufacturing method and/or equipment of semi-solid/liquid dosage forms that are not modified release

Changes to methods or equipment used in the manufacture of semi-solid or liquid products, where these are not modified release dosage forms and are not [sterile](#).

Conditions

- The product must not be a modified-release dosage form (including enteric-coated tablets, enteric capsules and transdermal patches) or sterile.
- The new manufacturing method and equipment must be validated consistent with applicable principles of the [Guide to Good Manufacturing Practice for Medicinal Products](#) and any relevant guidelines adopted by the TGA on at least one production-scale batch of the product.

Data requirements

You must submit:

- Details of the revised method of manufacture and/or equipment, and any relevant flow diagram of the new process.

You must generate the following data:

- Comparative batch data that demonstrates all results are comparable and within the same range as those obtained previously, as well as meeting currently approved drug product release specifications.
- For semi-solid and liquid products (for example, ointments, creams, lotions, oral liquids, moulded suppositories and pessaries), comparative batch data using appropriate current methodology demonstrating that there has been no change to the particle size distribution and polymorphic form of the API in suspension.
- These data are not required if the API is in solution for the drug product, or if it is in solution as liquid globules.

DMEO: Drug product manufacture - changes to manufacturing method and/or equipment of oral/nasal inhalation dosage forms that are not modified release

Changes to methods or equipment used in the manufacture of oral or nasal inhalation products, where these are not modified release dosage forms and are not [sterile](#).

Conditions

- The product must not be a modified-release dosage form (including enteric-coated tablets, enteric capsules and transdermal patches) or sterile.
- The new manufacturing method and equipment must be validated consistent with applicable principles of the [Guide to Good Manufacturing Practice for Medicinal Products](#) and any relevant guidelines adopted by the TGA on at least one production-scale batch of the product.

Data requirements

You must submit:

- Details of the revised method of manufacture and/or equipment, and any relevant flow diagram of the new process.

You must generate comparative batch data:

- That demonstrates all results are comparable and within the same range as those obtained previously, as well as meeting currently approved drug product release specifications.
- For the drug mass aerodynamic particle size distribution of the aerosol emitted by the drug product (for metered-dose pressurised inhalations, metered-dose nasal spray solutions, and dry powders for oral or nasal inhalation) that demonstrates that results are in the same range as previously obtained, as measured by either a multi-stage liquid impinger or a multi-stage cascade impactor (Andersen type).

DMES: Drug product manufacture - changes to manufacturing method and/or equipment for solid dosage forms that are not modified release

Changes to the manufacturing method or equipment used in the manufacture of solid dosage forms that are not modified release and are not [sterile](#).

Conditions

- The product must not be a modified-release dosage form (including enteric-coated tablets, enteric capsules and transdermal patches) or sterile.
- The new manufacturing method and equipment must be validated consistent with applicable principles of the [Guide to Good Manufacturing Practice for Medicinal Products](#) and any relevant guidelines adopted by the TGA on at least one production-scale batch of the product.

Data requirements

You must submit:

- Details of the revised method of manufacture and/or equipment, and any relevant flow diagram of the new process.

You must generate the following data:

- Comparative batch data that demonstrates all results are comparable and within the same range as those obtained previously, as well as meeting currently approved drug product release specifications.
- 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 for the drug product, or if it is in solution as liquid globules.

DMIT: Drug product manufacture - changes to in-process control tests and limits

Addition, revision or deletion of in-process control tests and associated limits applied during manufacture of the drug product.

Conditions

- The change must not relate to the parametric release of sterile products.

Parametric release

The European Pharmacopoeia refers to parametric release in the monograph “methods of preparation of sterile products” as:



When a fully validated terminal sterilisation method by steam, dry heat or ionising radiation is used, parametric release, that is the release of a batch of sterilised items based on process data rather than on the basis of submitting a sample of the items to sterility testing, may be carried out, subject to the approval of the competent authority.

Parametric release can only be applied to products terminally sterilised in their final containers.

- The change must be consistent with applicable principles of the [Guide to Good Manufacturing Practice for Medicinal Products](#).
- Any changes to in-process control test methods must be validated appropriately.
- The change must result in either improved quality or no change in the quality of the drug product.

Data requirements

You must submit:

- Details of the changes proposed, and the revised set of in-process control tests and limits. Test method details are not required.

You must generate the following data:

- Comparative batch data with the results within the same range as previously obtained.

DMRO: Drug product manufacture - reduction or removal of API and excipient overages for ingredients that are not antioxidants or similar

Reduction or removal of previously approved manufacturing overages for APIs or excipients, where the excipients may be preservatives but are not antioxidants and where the final drug product is not a modified release dosage form.

Since overages do not change the nominal quantity recorded in the ARTG, this type of change is not regarded as a change in the product formulation.

Conditions

- Any excipient involved must not be an antioxidant or another ingredient whose function (at least in part) involves being 'consumed' over time.
- Manufacture of the product with reduced overage must be appropriately validated.
- The TGA must be notified as a priority if the results of supporting stability data fail to meet the specifications. The TGA reserves the right to withdraw the product from the market if this requirement is not met.

Data requirements

You must submit:

- The revised manufacturing formula.

You must generate the following data:

- Comparative batch data to demonstrate that the results are comparable to those obtained previously (allowing for the reduction in overage).
- Stability data on at least one production batch of the post-variation product (with at least two more production batches to be similarly tested).

DMSE: Drug product manufacture - changes to manufacturing method and/or equipment of sterile dosage forms that are not modified release

Changes to methods or equipment used in the manufacture of sterile dosage forms, where these are not modified release dosage forms.

Conditions

- The product must not be a modified-release dosage form.
- The new manufacturing method and equipment must be validated consistent with applicable principles of the [Guide to Good Manufacturing Practice for Medicinal Products](#) on at least one production-scale batch of the product.
- Other changes to ensure sterility are permitted, provided that:
 - the technology to be used already exists at the manufacturing site and is in use for other TGA-approved products.
 - there are no changes to (or there are improvements in) microbiological environmental standards, bioburden specifications, the sterilisation cycle or its parameters, and sterility assurance levels.

Data requirements

You must submit:

- Details of the revised method of manufacture and/or equipment, and any relevant flow diagram of the new process.
- Validated process times.

You must generate the following data:

- Comparative batch data that demonstrates all results are comparable and within the same range as those obtained previously, as well as meeting currently approved drug product release specifications.
- The new method of manufacture (including sterilisation of containers or container components, and use of a second filter in a filling line) or new manufacturing equipment (such as introduction of a similar filling line) must not affect the final sterility of the product.
- All of the dosage-specific data requirements described in the following variation types must be certified as having been met, as appropriate:
 - For solid dosage forms, see [DMES: Drug product manufacture - changes to manufacturing method and/or equipment of solid dosage forms that are not modified release](#).
 - For semi-solid/liquid dosage forms, see [DMEL: Drug product manufacture - changes to manufacturing method and/or equipment of semi-solid/liquid dosage forms that are not modified release](#).
 - For oral/nasal inhalation dosage forms, see [DME0: Drug product manufacture - changes to manufacturing method and/or equipment of oral/nasal inhalation dosage forms that are not modified release](#).

1.2.3 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.

DMDS: 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.

Requires update to ARTG data: Visual Identification



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.

- Where a change involves product shape, dimension or embossing/debossing, the comparative dissolution profiles of pre-variation and post-variation products should be similar (that is, the f_2 value should be between 50 and 100).

'Comparative dissolution profiles' should be generated on three recent pre-variation batches and at least one batch of post-variation product as follows:

- At least 12 dosage units (for example, tablets, capsules) of each batch should be tested individually, and mean and individual results reported. The percentage of nominal content released should be measured at a minimum of three suitably spaced time points (excluding the zero time point) to provide a profile for each batch (for example, at 5, 15, 30 and 45 minutes, or as appropriate to achieve virtually complete dissolution). The batches should be tested using the same apparatus and, if possible, on the same day. Test conditions should be those used in routine quality control or, if dissolution is not part of routine quality control, any reasonable, validated method.
- To demonstrate the similarity of two dissolution profiles, the similarity factor, f_2 , should be calculated using the equation and conditions stated in Appendix I of the European Medicines Agency (EMA) [Guideline on the Investigation of Bioequivalence \(CPMP/EWP/QWP/1401/98 Rev. 1/Corr\)](#). The f_2 value should be between 50 and 100. In cases where more than 85% of the active substance is dissolved within 15 minutes in all tested batches, dissolution profiles are considered to be similar and the similarity factor does not need to be calculated.
- Insufficient quantities of recently manufactured batches may be available to meet this requirement. In these cases, it is acceptable to test retention batches, and to explain in the test report why this was done, stating the age and storage history of the samples.

Data requirements

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.

1.2.4 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.

DMCM: Drug product manufacture – changes to the method of manufacture

Any proposed changes to the method of manufacture of the drug product can be submitted as part of this Category 3 variation type. This includes changes to batch size and equipment.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- A detailed description of the changed manufacturing process, including in-process controls.
- Process validation protocols and process validation data for the changed process (including validation of sterile manufacture and sterilisation processes, if applicable) for at least three production-scale batches. If fewer than three batches are process validated, explain why.
- Batch data for representative batches of the drug product manufactured using the current and proposed process.
 - At least one of these batches should be full production scale unless otherwise justified; the other batches should be at least pilot scale but manufactured using full production-scale equipment unless otherwise justified.
 - These data should be compared with at least three batches of recently manufactured pre-variation product. All data should be generated using approved routine quality control methods, unless otherwise justified and details are provided of the non-routine methods used.
- Relevant comparative data of the type listed below for the dosage form manufactured using the new and old manufacturing method or process.

At least three recently manufactured batches of the pre-variation product and at least 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.

- For all **solid dosage forms** (for example, tablets, capsules, compressed pessaries/suppositories, implants, modified-release dosage forms) and transdermal patches, dissolution profiles using a discriminatory method. For modified-release dosage forms and low-solubility drugs used in conventional dosage form, dissolution testing over a pH range (for example, at pH 1.0, 4.5 and 6.8) should be conducted, unless otherwise justified. Similarity factors (f_2) should be calculated, where appropriate.
 - For **semi-solid and liquid suspension products**, particle size data (microscopic imaging or other methods) and/or dissolution data, as relevant.
 - For metered-dose pressurised inhalations (oral or nasal), dry powder for inhalation products, and metered-dose nasal spray solutions or suspensions, drug mass aerodynamic particle size distribution data using a multi-stage liquid impinger or a multi-stage cascade impactor of the Andersen type.
- Stability data, or confirmation that stability data will be generated. Relevant stability data should be generated for batches produced using the new process, as required by GMP.

The TGA may ask the sponsor to provide accelerated stability data for a particular medicine if stability is known to be a problem or if changes in stability could have clinical consequences. The relevant stability data do not necessarily need to be supplied before the change of process is approved. However, if the data are not supplied, the sponsor should provide written assurance that stability data will be generated, and the TGA should be notified immediately if there are any significant problems, or if the data indicate that the stability of product from the new process is different from that made by the original process to the extent that the shelf life of the medicine would be affected.

- If the changes proposed may affect bioavailability of the product, bioavailability data establishing bioequivalence of product manufactured using the new and currently approved processes, or a justification for a waiver for such data. For further information on this aspect, see [Guidance 15: Biopharmaceutical studies](#). If bioavailability data are required and are submitted to support the change, the application becomes a Category 1 application.

1.3 Drug product - site of manufacture changes

1.3.1 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 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 information on changes that do not require prior approval in [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

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.

Data requirements

You must submit:

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

1.3.2 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.

DMDM: Drug product site of manufacture - cessation of a site or deletion of a manufacturing step

Cessation of, or deletion of a step in, the manufacture of the drug product at an approved site.

Requires update to ARTG data: Manufacturers

Conditions

- This change is applicable to all medicines, including sterile products and modified-release dosage forms.
- There must be at least one other site that performs the same steps of manufacture as the ceased site, or that performs the deleted step of manufacture.

Data requirements

You must submit:

- The name and address of the manufacturer to be ceased.
- Details of the manufacturing step(s) to be deleted, as relevant.
- Documentary evidence to show that there is at least one registered site of manufacture performing the same step of manufacture as the ceased site.

DMPL: Drug product site of manufacture - change to site of labelling/primary packaging (non-sterile products) or labelling/secondary packaging

Change to the location of a manufacturer, or addition of a new manufacturer, approved for labelling and primary packaging operations for non-sterile dosage forms or labelling and secondary packaging operations for all dosage forms.

Requires update to ARTG data: Manufacturers

Conditions

- A change in, or addition of an alternative, site of **primary packaging** operations may relate to any product except products that are sterile or are manufactured under sterile conditions.
- A change in, or addition of an alternative, site of **secondary packaging** operations may relate to any product, including sterile products and products manufactured under sterile 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 must be no change to any aspect of the quality data other than changes to manufacturing equipment.
 - Where a change in manufacturing equipment is made, this must be validated in accordance with the principles of GMP.

Data requirements

You must submit:

- The name and address of the new manufacturer and licence/clearance number.
- Details of the manufacturing step(s) undertaken at the new site of manufacture.

DMSL: Drug product site of manufacture - change to site of manufacture of non-sterile semi-solid/liquid dosage forms that are not modified release

Change to the location of an approved manufacturer, or addition of a new manufacturer, to make the final drug product, where the products are non-sterile, semi-solid or liquid dosage forms that are not modified release.

Requires update to ARTG data: Manufacturers

Conditions

- Applies to sites of manufacture of the final drug product only, not sites performing in-process steps.
- The product must not be sterile or manufactured under sterile conditions.
- The product must not be a modified-release dosage form. This includes enteric-coated tablets, enteric capsules and transdermal patches.
- 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 must be no changes to any aspect of the quality data other than changes to manufacturing equipment or method at the new site of manufacture and
 - The changes to the manufacturing methods are only those necessitated by scale-up or downscaling, e.g. use of different-sized equipment or
 - The change does not adversely affect the reproducibility of the process and it is not the result of unexpected events arising during manufacture or because of stability concerns.
 - Where a change in manufacturing equipment or method is made, this must have been validated at the new manufacturing site in accordance with the principles of GMP and/or any relevant guidelines adopted by the TGA.

Data requirements

You must submit:

- The name and address of the new manufacturer and licence/clearance number.
- Details of the manufacturing step(s) undertaken at the new site of manufacture.
- A summary of the change in manufacturing equipment or manufacturing method at the new site, if relevant.

You must generate the following data:

- Comparative batch data demonstrating all results are comparable and within the same range as those obtained previously, as well as meeting currently approved drug product release specifications.

- For semi-solid and liquid products (for example, ointments, creams, lotions, oral liquids, moulded suppositories and pessaries), comparative batch data using appropriate current methodology demonstrating that there has been no change to the particle size distribution and polymorphic form of the API in suspension. 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.
- Appropriate validation of the manufacturing process at the new site carried out on at least one production-scale batch. The second and third production-scale batches should be subsequently validated.

DMSO: Drug product site of manufacture - change to site of manufacture of non-sterile oral/nasal inhalation dosage forms that are not modified release

Change to the location of an approved manufacturer, or addition of a new manufacturer, to make the final drug product, where the products are non-sterile oral or nasal inhalation dosage forms that are not modified release.

Requires update to ARTG data: Manufacturers

Conditions

- Applies to sites of manufacture of the final drug product only, not sites performing in-process steps. For changes to the site of manufacture not involving the final product see:
 - [Excipients \(not of animal or human origin\) - changes to the manufacturing process and/or site \(same specifications\)](#) or
 - [Non-sterile container - changes to the supplier or manufacturer if same material and specification.](#)
- The product must not be sterile or manufactured under sterile conditions.
- The product must not be a modified-release dosage form.
- 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 must be no changes to any aspect of the quality data other than changes to manufacturing equipment or method at the new site of manufacture.
 - Where a change in manufacturing equipment or method is made, this must have been validated at the new manufacturing site in accordance with the principles of GMP and/or any relevant guidelines adopted by the TGA.

Data requirements

You must submit:

- The name and address of the new manufacturer and licence/clearance number.
- Details of the manufacturing step(s) undertaken at the new site of manufacture.

- A summary of the change in manufacturing equipment or manufacturing method at the new site, if relevant.
- A declaration that the changes to the manufacturing methods are only those necessitated by scaling-up or down, e.g. use of different-sized equipment, that the change does not adversely affect the reproducibility of the process, that it is not the result of unexpected events arising during manufacture or because of stability concerns.

You must generate the following data:

- Comparative batch data demonstrating all results are comparable and within the same range as those obtained previously, as well as meeting currently approved drug product release specifications.
- For metered-dose pressurised inhalations, metered-dose nasal spray solutions, and dry powders for oral or nasal inhalation, the comparative batch data for the drug mass aerodynamic particle size distribution of the aerosol emitted by the drug product demonstrating that results are in the same range as previously obtained, as measured by either a multi-stage liquid impinger or a multi-stage cascade impactor (Andersen type).

DMSS: Drug product site of manufacture - change to site of manufacture of non-sterile solid dosage forms that are not modified release

Change to the site of an approved manufacturer, or addition of a new manufacturer, to make the final drug product, where the products are non-sterile solid dosage forms that are not modified release.

Requires update to ARTG data: Manufacturers

Conditions

- Applies to sites of manufacture of the final drug product only, not sites performing in-process steps.
- The product must not be sterile or manufactured under sterile conditions.
- The product must not be a modified-release dosage form. This includes enteric-coated tablets, enteric capsules and transdermal patches.
- 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 must be no changes to any aspect of the quality data other than changes to manufacturing equipment or method at the new site of manufacture as outlined under [Site of manufacture changes](#).
 - Where a change in manufacturing equipment or method is made, this must have been validated at the new manufacturing site in accordance with the principles of GMP and/or any relevant guidelines adopted by the TGA.

Data requirements

You must submit:

- The name and address of the new manufacturer and licence/clearance number.
- Details of the manufacturing step(s) undertaken at the new site of manufacture.
- A summary of the change in manufacturing equipment or manufacturing method at the new site, if relevant.
- A declaration that the changes to the manufacturing methods are only those necessitated by scaling-up or down, e.g. use of different-sized equipment, that the change does not adversely affect the reproducibility of the process, that it is not the result of unexpected events arising during manufacture or because of stability concerns.

You must generate the following data:

- Comparative batch data demonstrating all results are comparable and within the same range as those obtained previously, as well as meeting currently approved drug product release specifications.
- 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.
- Appropriate validation of the manufacturing process at the new site carried out on at least one production-scale batch. The second and third production-scale batches should be subsequently validated.

DMTR: Drug product site of manufacture - change to site performing testing and release for supply

Change to the location of a manufacturer, or addition of a new manufacturer, approved for quality control testing (including sterility, microbiological, chemical, physical and bacterial endotoxin or pyrogen testing) or release for supply of the final drug product.

Requires update to ARTG data: Manufacturers

Conditions

- The change applies to sites of manufacture of the final drug product only, not sites performing in-process steps.
- This change is applicable to all medicines, including sterile products and modified-release dosage forms.
- 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 may not be any changes to the existing test methods used for testing the product, whether or not the test methods have been provided to the TGA previously, except where allowed by [DMSL: Drug product site of manufacture - change to site of manufacture of non-sterile semi-solid/liquid dosage forms that are not modified release](#).

Data requirements

You must submit:

- The name and address of the new manufacturer and licence/clearance number.
- Details of the manufacturing step(s) undertaken at the new site of manufacture.

You must generate the following data:

- Appropriate technology transfer of the approved test methods to the proposed site must have been carried out.

1.3.3 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.

DMCS: Drug product site of manufacture - changes to the site(s) of manufacture

Any proposed changes to the site of manufacture of the drug product can be submitted as part of this Category 3 variation type.

Requires update to ARTG data: Manufacturers

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- GMP evidence for the new site (that is, the Australian manufacturing licence for an Australian site, or a current GMP clearance for an overseas site). The Australian licence or GMP clearance should cover the relevant manufacturing steps and must be valid (before expiry) at the time of application.
- A declaration that the manufacturing process, including batch size, is the same as that used at the currently approved manufacturing sites, or a description of any differences between the processes at the new and currently approved sites.
- Appropriate validation of the process at the new site for at least one production-scale batch (including validation of sterile manufacture and sterilisation processes, if applicable) to demonstrate that 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 representative batches of drug product that were manufactured at both the currently approved site and the new site. At least one batch from the new site should be full production scale unless otherwise justified; other batches should be at least pilot scale and manufactured using full production-scale equipment.
- Relevant comparative data on the product (see [DMCM: Drug product manufacture – changes to the method of manufacture](#)). For modified-release dosage form and for low-solubility drugs used in conventional dosage form, dissolution testing over a pH range (for example, at pH 1.0, 4.5 and 6.8) should be considered, unless justification can be provided for not conducting such testing. Similarity factor, f_2 , should be calculated, where appropriate.

- Relevant stability data should be generated for batches produced at the new site, as required by GMP. The TGA may ask the sponsor to provide accelerated stability data for a particular medicine if stability is known to be a problem or if changes in stability could have clinical consequences. The relevant stability data do not necessarily need to be supplied before the change of site is approved. However, if stability data are not supplied, the sponsor should provide written assurance that stability data will be generated, and the TGA should be notified as a priority if there are any significant problems, or if the data indicate that the stability of product from the new site is different from that made at the original site to the extent that the shelf life of the medicine would be affected.

1.4 Drug product formulation changes

1.4.1 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 [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#) for further information.

CAAO: Correct an ARTG entry - Animal origin

Requires update to ARTG data: Formulation.

Conditions

- Data is submitted as described below.

Data requirements

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

Requires update to ARTG data: Formulation.

Conditions

- Data is submitted as described below.

Data requirements

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.

1.4.2 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](#) because they create a separate and distinct good. However, the existing AUST R number can be retained under the provisions of the [Therapeutic Goods \(Groups\) Order No. 1 of 2001](#).

The conditions outlined below the description of each variation type must be met for the request to be processed as self-assessable. All other formulation changes require the submission of data for TGA evaluation. See [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#) or [DFNA: Formulation changes \(CE\) – New AUST R number](#).

DFCI: Formulation - addition or deletion of, or variation to, an inked imprint

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

Requires update to ARTG data: Formulation.

Note: 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 [DMDS: Drug product manufacture - changes to dimensions, shape, inked imprint, embossing or debossing of solid dosage forms](#).

Conditions

- Any new colour or ink should be 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 must already be present in another prescription medicine registered on the ARTG.
- If relevant, the drug product specification should be revised to incorporate any change in product description.
- The new markings do not reduce product differentiation or cause confusion.

Data requirements

You must submit:

- 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](#)).
- The revised product description (if this has changed), incorporated into the revised set of drug product specifications (release and expiry).
- The ingredient number for the new proprietary excipient, together with the ARTG number of the existing good that contains that ingredient, if relevant.
- An updated [CPD document](#) that incorporates the changes, if applicable.
- Revised labels, stating 'New Appearance' if applicable.
- A clean copy of the PI. Where the proposed change would involve amendment of a PI, a marked-up copy should also be provided.

Associated changes

You may need to update other information about your medicine as a result of the changes to the inked imprint. Associated variation types that you can include with DFCI are:

- [ZFSM: ARTG data - Manufacturer changes associated with DFCI or DFFC](#)
- [ZFSV: ARTG data - Visual identification changes associated with DFCI or DFFC](#).

DFFC: Formulation - change relating to 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.

Requires update to ARTG data: Formulation.

Note: If the colouring agent, flavour or fragrance is present at more than 2% w/w or w/v, this requires evaluation of data. See variation type DFCF: Formulation – changes (CE) – Retaining AUST R number.

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 must already be present in another prescription medicine registered on the ARTG.
- There are only changes to, or addition or deletion of excipients that are colours, flavours or fragrances. You should consider if the formulation of a proprietary excipient contains excipients that are not colours, flavours or fragrances.
- The changes do not reduce differentiation or cause confusion.
- 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.

Data requirements

You must submit:

- The ingredient number for the new proprietary excipient, together with the ARTG number of the existing good that contains that ingredient, 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](#)).
- Updated specifications, if applicable.
- An updated [CPD document](#) that incorporates the changes, if applicable.
- Revised labels, stating 'New Appearance' or 'New Formulation' if applicable.

- A clean copy of the PI. Where the proposed change would involve amendment of a 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.

Associated changes

You may need to update other information about your medicine as a result of the changes to the colour, flavour or fragrance. Associated variation types that you can include with DFFC are:

- [ZFSM: ARTG data - Manufacturer changes associated with DFCI or DFFC](#)
- [ZFSV: ARTG data - Visual identification changes associated with DFCI or DFFC](#).

1.4.3 Category 3 requests - Data evaluation required under s. 23 (separate and distinct good) – Retaining AUST R number

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

DFCF: Formulation – changes (CE) – Retaining AUST R number

Proposed changes to the excipients in the drug product where the [Therapeutic Goods \(Groups\) Order No. 1 of 2001](#) allows the AUST R number to be retained.

Requires update to ARTG data: Formulation.



The AUST R number can be retained

Under s. 16(1) of the [Therapeutic Goods Act 1989](#), a change in formulation means that the reformulated 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, for certain types of formulation changes.

The following formulation changes allow the current AUST R number to be retained:

- removal or addition of fragrance, flavour, ink or colour
- change in existing quantity of excipients (but not total removal).

Any other formulation changes will result in a new AUST R number, see variation type [DFNA: Formulation - changes \(CE\) – New AUST R number](#).

Conditions

- An excipient can only be removed from the formulation if it is a flavour, ink or colour.

Data requirements

This list of what to submit is not exhaustive and represents the minimum data necessary for assessment. The TGA can request additional data or information from you in support of your application.

You must submit:

- A copy of the current and revised formulation, and details of any new manufacturing process and associated validation data.
- 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](#)).
- Details of the specifications applicable to all the excipients used in the new formulation. If an excipient was not used in the previous formulation, certificates of analysis issued by the drug product manufacturer for two or three representative batches of the excipient should be submitted.
- For excipients that are of ruminant origin:
 - For all products that are implanted, injected or given by parenteral, ophthalmic or intra-tracheal routes of administration, details of excipients derived from [Category IC tissues](#) from transmissible spongiform encephalopathy (TSE)-relevant ruminant species (including excipients whose manufacture may have exposed them to Category IC materials) and measures taken by the manufacturers to minimise TSE risk.
 - For products that are given by the oral, topical, vaginal, rectal or inhalation routes that contain excipients derived from [Category A or B materials](#) (including excipients whose manufacture may have exposed them to Category A or B materials) from TSE-relevant ruminant species, details of all such excipients and measures taken by the manufacturers to minimise TSE risk.

- Products given by the oral, topical, vaginal, rectal or inhalation routes that contain only excipients derived from Category IC TSE-relevant ruminant materials, details of the excipients and a declaration that the Category IC material has been self-assessed and complies with the TGA's [Supplementary information on Transmissible Spongiform Encephalopathies regulation](#), together with an assurance that the sponsor will maintain a record of compliance for future TGA compliance checks.
- Current Certificate of Suitability (CEP) issued by the European Directorate for the Quality of Medicines and HealthCare (EDQM) to the manufacturer of the excipient. Not all CEPs from the EDQM will be acceptable; this depends on the source country of the animal and the parts of the animal used to manufacture the excipient, where relevant.
- Refer to [Guidance 10: Adventitious agent safety of medicines](#) for additional detail on requirements for ingredients of human or animal origin.
- Relevant comparative data for the proposed new and currently approved drug products to demonstrate that the change in formulation does not lead to changes in the physical characteristics of the product that may affect the absorption and *in vivo* effect of the medicine. For further guidance, see [DMCM: Drug product manufacture – changes to the method of manufacture](#).
- Where the change in formulation involves introduction of, or variation to, a range of values for particular excipients, relevant validation of the manufacture and testing of the product with excipient content at the extremes of the range may be required. Relevant guidance can be found in the current Committee for Proprietary Medicinal Products (CPMP) guidance document [CPMP/QWP/486/95: Note for guidance on manufacture of the finished dosage form](#) adopted by the TGA.
- Certificates of analysis for at least one production-scale batch of the drug product manufactured using the proposed new formulation. Pilot-scale batches are acceptable, if justified.
- Stability data in accordance with relevant EMA/ICH guidelines. For minor formulation changes, the sponsor may justify why relevant stability data need not be provided for review. However, a commitment to carry out stability testing on at least three production-scale batches of the reformulated product is required.
- Comparative bioavailability data may be required to establish bioequivalence of the new and currently approved formulation (for example, if significant changes to the formulation are made and this is likely to affect the bioavailability of the product). However, a justification may be provided to demonstrate why such a study is not required. If bioequivalence data are submitted, the application will be re-categorised as a Category 1 application. (For further information on changes that are unlikely to affect bioavailability and provision of a justification in lieu of bioavailability/bioequivalence data, see [Guidance 15: Biopharmaceutic studies](#)).
- If the new formulation involves a change to the preservative system, additional data may be required. These may include stability data (including microbial quality and proof of antimicrobial efficacy of the drug product at expiry) and test methods (with accompanying validation data) for determination of preservative content in the drug product. For additional information, please refer to [TGO 100 - Microbiological standards for medicines](#). If relevant, revised labels may be required to provide information on the new formulation.
- A clean copy of the PI must be provided. Where the proposed change would involve amendment of a PI, a marked-up copy should also be provided, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

Associated changes

You may need to update other information about your medicine as a result of the changes to the excipients in the formulation. Associated variation types that you can include with DFCF are:

- [ZFRG: ARTG data – Container and shelf life changes associated with DFCF/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRM: ARTG data – Manufacturer changes associated with DFCF/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRN: ARTG data – Good name changes associated with DFCF/PFCF – Retaining AUST R number](#)
- [ZFRO: Other consequential changes to the dossier associated with DFCF/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRP: ARTG data – Pack size and poison schedule changes associated with DFCF/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRS: ARTG data – Sterility changes associated with DFCF/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRV: ARTG data - Visual identification changes associated with a result of DFCF/PFCF or DTTR – Retaining AUST R number.](#)

1.4.4 Category 3 requests — Data evaluation required under s. 23 (separate and distinct good) – New AUST R number

These variations fall under s. 23 of the [Therapeutic Goods Act 1989](#) and require the submission of data for evaluation.

DFNA: Formulation changes (CE) – New AUST R number

Proposed changes to the formulation of the drug product which results in goods that require a new AUST R number.

Requires update to ARTG data: Formulation.



The AUST R number cannot be retained

Under s. 16(1) of the [Therapeutic Goods Act 1989](#), a change in formulation means that the reformulated product is a separate and distinct good from the existing product, and this requires a new ARTG entry. The [Therapeutic Goods \(Groups\) Order No. 1 of 2001](#) only applies for certain types of formulation changes.

For formulation changes that allow the AUST R number to be retained, see variation type [DFCF: Formulation changes \(CE\) – Retaining AUST R number](#).

Conditions

- Data is submitted as described below.

Data requirements

This list of what to submit is not exhaustive and represents the minimum data necessary for assessment. The TGA can request additional data or information from you in support of your application.

You must submit:

- A copy of the current and revised formulation, and details of any new manufacturing process and associated validation data.
- 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](#)).
- Details of the specifications applicable to all the excipients used in the new formulation. If an excipient was not used in the previous formulation, certificates of analysis issued by the drug product manufacturer for two or three representative batches of the excipient should be submitted.
- For excipients that are of ruminant origin:
 - For all products that are implanted, injected or given by parenteral, ophthalmic or intra-tracheal routes of administration, details of excipients derived from [Category IC tissues](#) from transmissible spongiform encephalopathy (TSE)-relevant ruminant species (including excipients whose manufacture may have exposed them to Category IC materials) and measures taken by the manufacturers to minimise TSE risk.
 - For products that are given by the oral, topical, vaginal, rectal or inhalation routes that contain excipients derived from [Category A or B materials](#) (including excipients whose manufacture may have exposed them to Category A or B materials) from TSE-relevant ruminant species, details of all such excipients and measures taken by the manufacturers to minimise TSE risk.
 - Products given by the oral, topical, vaginal, rectal or inhalation routes that contain only excipients derived from Category IC TSE-relevant ruminant materials, details of the excipients and a declaration that the Category IC material has been self-assessed and complies with the TGA's [Supplementary information on Transmissible Spongiform Encephalopathies regulation](#), together with an assurance that the sponsor will maintain a record of compliance for future TGA compliance checks.
 - Current Certificate of Suitability (CEP) issued by the European Directorate for the Quality of Medicines and HealthCare (EDQM) to the manufacturer of the excipient. Not all CEPs from the EDQM will be acceptable; this depends on the source country of the animal and the parts of the animal used to manufacture the excipient, where relevant.
 - Refer to [Guidance 10: Adventitious agent safety of medicines](#) for additional detail on requirements for ingredients of human or animal origin.
- Relevant comparative data for the proposed new and currently approved drug products to demonstrate that the change in formulation does not lead to changes in the physical characteristics of the product that may affect the absorption and *in vivo* effect of the medicine. For further guidance, see [DMCM: Drug product manufacture – changes to the method of manufacture](#).
- Where the change in formulation involves introduction of, or variation to, a range of values for particular excipients, relevant validation of the manufacture and testing of the product with excipient content at the extremes of the range may be required. Relevant guidance can

be found in the current Committee for Proprietary Medicinal Products (CPMP) guidance document [CPMP/QWP/486/95: Note for guidance on manufacture of the finished dosage form](#) adopted by the TGA.

- Certificates of analysis for at least one production-scale batch of the drug product manufactured using the proposed new formulation. Pilot-scale batches are acceptable, if justified.
- Stability data in accordance with relevant EMA/ICH guidelines. For minor formulation changes, the sponsor may justify why relevant stability data need not be provided for review. However, a commitment to carry out stability testing on at least three production-scale batches of the reformulated product is required.
- Comparative bioavailability data may be required to establish bioequivalence of the new and currently approved formulation (for example, if significant changes to the formulation are made and this is likely to affect the bioavailability of the product). However, a justification may be provided to demonstrate why such a study is not required. If bioequivalence data are submitted, the application will be re-categorised as a Category 1 application. (For further information on changes that are unlikely to affect bioavailability and provision of a justification in lieu of bioavailability/bioequivalence data, see [Guidance 15: Biopharmaceutic studies](#)).
- If the new formulation involves a change to the preservative system, additional data may be required. These may include stability data (including microbial quality and proof of antimicrobial efficacy of the drug product at expiry) and test methods (with accompanying validation data) for determination of preservative content in the drug product. For additional information, please refer to [TGO 100 - Microbiological standards for medicines](#). If relevant, revised labels may be required to provide information on the new formulation.
- A clean copy of the PI must be provided. Where the proposed change would involve amendment of a PI, a marked-up copy should also be provided, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

Associated changes

You may need to update other information about your medicine as a result of the changes to the formulation. Associated variation types that you can include with DFNA are:

- [ZFNC: ARTG data – Container and shelf life changes associated with DFNA/PFNA – For the new AUST R number](#)
- [ZFNM: ARTG data – Manufacturer changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNN: ARTG data – Good name changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNO: Other consequential changes to the dossier associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNP: ARTG data – Pack size and poison schedule changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNS: ARTG data – Sterility changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNV: ARTG data – Visual identification changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)

1.5 Drug product specifications or test changes



Certified product details (CPD) documents

An updated [CPD document](#) is usually provided when a change is made to aspects of the drug product specifications, such as test requirements, limits of acceptance or non-pharmacopoeial test methods.

If a self-assessable request results in changes to the product specifications or the non-pharmacopoeial test methods, an updated and complete [CPD document](#) must be provided in PDF format at the time of the request.

1.5.1 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.

DSAM: Drug product specification - changes to non-biological assay method for an active or excipient that is not a radiopharmaceutical

Changes to a non-biological method used for assaying the API or excipients in a final drug product that is not a radiopharmaceutical.

Conditions

- The product must not be a radiopharmaceutical.
- If the results obtained using the proposed method do not agree with the results obtained during TGA testing, using an official method, the results from the official method will be deemed to be correct.
- The proposed method must not be a biological method.
- The proposed method must not be a test method for impurities, related substances or degradation products.
- Validation data from the proposed method must demonstrate either:
 - an improvement in at least one of precision, accuracy or specificity, without a reduction in the other parameters or
 - an improvement in specificity or accuracy with reduced precision (providing precision remains within the specified limits).

Data requirements

You must submit:

- Details of the proposed test method.

You must generate the following data:

- Appropriate validation data for the proposed method.

DSID: Drug product specification - changes to identification tests for the active or excipient

Changes to the tests used to identify the API or excipients in the final drug product.

Conditions

- The changes to identification tests must:
 - be from a less specific to a more specific identification test (for example, from an ultraviolet/visible spectrophotometric or chromatographic method—such as thin layer chromatography, gas chromatography or high-performance liquid chromatography (HPLC) —to a conventional infrared spectroscopic method) and/or
 - vary the existing identification test (for example, an HPLC test that demonstrably improves or at least maintains the specificity of the method) and/or
 - replace an existing identification test with a near infrared spectroscopic identification test and/or
 - include a new identification test in addition to an existing identification test.
- The method must be appropriately validated.
- Any additional identification test included cannot serve as an alternative identification test (this should be submitted as a Category 3 application).
- If near-infrared spectroscopy is used, the method development and other data requirements (including data collection, establishment of the spectral reference library, calibration and validation of the method) must comply with the [current EMA guideline](#) on use of near-infrared spectroscopy that has been adopted by the TGA.

Data requirements

You must submit:

- Details of the changes to the existing test or the new identification test.
- The revised set of drug product specifications at release and expiry.

You must generate the following data:

- Appropriate validation data for the identification test.

DSIP: Drug product specification - changes from an in-house test method to a pharmacopoeial test method

Changes to the specifications to ensure that the drug product complies with the requirements of a default standard (i.e. a monograph in the BP, USP-NF or EP), where previously no default standard applied.

Conditions

- Any changes can be made to assay and/or related substances test methods, but not to a dissolution method which requires TGA evaluation of supporting data.
- The method must be appropriately validated.

Data requirements

You must submit:

- A summary description of the change and details of the new method.

You must generate the following data:

- Equivalency of the current and pharmacopoeial test method must be established by testing of three batches of the drug product using the current and proposed methods.

DSNL: 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 proposed limits must be consistent with applicable official standards or adopted guidelines.
- There must be no change in test methods other than those allowed under change types:
 - [DSAM: Drug product specification - changes to non-biological assay method for an active or excipient that is not a radiopharmaceutical](#)
 - [DSIP: Drug product specification - changes from an in-house test method to a pharmacopoeial test method](#)
 - [DSPT: Drug product specification - changes resulting from pharmacopoeial or TGO requirements](#)
 - [DSPL: Drug product specification - minor changes to physicochemical test methods and limits](#)

Data requirements

You must submit:

- A statement of the current and proposed limits.
- The revised set of drug product specifications at release and expiry.

DSNT: Drug product specification - addition of test and limit

Addition of a new test and associated limits to the approved specifications for the final drug product.

Conditions

- The proposed method must be validated.
- The proposed limit (release and expiry) of the new test must be based on batch data obtained at product release and on storage for the duration of the shelf life of the product. The limit must comply with any applicable official standard, TGO or adopted guidelines.

Data requirements

You must submit:

- A statement of the new test and limit.
- The revised set of product specifications at release and expiry.
- Details of the test method.

You must generate the following data:

- Appropriate validation data for the test method.

DSPL: Drug product specification - minor changes to physicochemical test methods and limits

Minor changes to methods used to test physicochemical parameters of the final drug product.



Physicochemical parameters include pH, hardness, friability, colour, particle size distribution, particulate matter contamination, density, specific gravity, optical rotation, extractable volume, osmolality, osmolarity and viscosity.

Conditions

- The test limit should either remain unchanged or be more stringent.
- The amended method should have been validated.

Data requirements

You must submit:

- Details of the new method together with a summary description of the change.

You must generate the following data:

- Appropriate validation data for the new method.

DSPT: Drug product specification - changes resulting from pharmacopoeial or TGO requirements

Changes to the specifications for the final drug product as a result of amendments to requirements in a default standard (i.e. a monograph in the BP, USP-NF or EP), or relevant requirements in an applicable standard made by the Minister under section 10 of the [Act](#).

Conditions

- The products must currently be tested to the existing pharmacopoeial or Therapeutic Goods Order (TGO) requirements.
- Any tests that are performed in addition to those of the pharmacopoeial monograph or TGO must continue to be performed.
- The requirements applied from one pharmacopoeia must not be changed to another, except where the changes are allowed by other sections of this document (e.g. changing from USP to BP is not permitted as a notification).
- The new pharmacopoeial monograph or amended TGO must be applicable to the product and, if necessary, appropriate validation data must be generated.
- If the change involves updating microbiological test requirements for non-sterile products to meet the [TGO 100 - Microbiological standards for medicines](#), the product must have undergone a risk assessment for objectionable microorganisms in addition to those specified in the pharmacopoeias that form the basis of the TGO.

Data requirements

You must submit:

- The revised set of drug product specifications (release and expiry), if applicable.

- If the change relates to an update to meet the requirements of the [TGO 100 - Microbiological standards for medicines](#), a written assurance that the TGA can review the risk assessment report for objectionable microorganisms other than those specified in the order, if required.

You must generate the following data:

- Appropriate validation data, as required.

DSST: Drug product specification - changes to sterility test method

Changes to the sterility test methods used for the final drug product.

Conditions

- All aspects of the test must comply with the requirements of the internationally harmonised test published in a default pharmacopoeia and as specified in [TGO 100 - Microbiological standards for medicines](#).
- The change must comply with the guidelines on particular aspects of the sterility test that are outlined in [Guidance 17 - Microbial quality of prescription and over-the-counter medicines](#).

Data requirements

You must submit:

- Details of the new method together with a summary description of the change.

1.5.2 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.

DSCS: Drug product specifications - changes to specifications, including changes to test methods

Any proposed changes to the specifications of the drug product can be submitted as part of this Category 3 variation type.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- A copy of the revised specifications at release and expiry.
- Justification for the proposed changes, including changes to test methods.
- Validation of any changed test methods. Method cross-validation data against alternative or pharmacopoeial methods may also be required, if relevant.
- Certificates of analysis for at least two representative production-scale batches of the drug product that demonstrate the product manufacturer's ability to meet the revised specifications. If pilot-scale batches were used for testing, this should be explained and justified. Where appropriate, batch analytical data from aged samples may be necessary—for example, to demonstrate compliance throughout shelf life.

1.6 Excipients changes



Definition and conditions

An **excipient** is any component of a drug product other than the active pharmaceutical ingredient.

Except as specified in [EMRS](#) below, changes to excipients of biological origin (animal or human source) may not be made as a notification.

1.6.1 Changes that do not require reporting to the TGA

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

Excipients (not of animal or human origin) - changes to the manufacturing process and/or site (same specifications)

You do not need to notify the TGA if you are making a variation that changes the manufacturing process and site of manufacture of excipients of the same specifications (but excluding excipients of animal or human origin).

1.6.2 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.

EMRS: Excipient manufacture (from Category IC ruminant tissues) - changes in source (from animal to non-animal) and/or manufacturing process or site

Changes to the source, manufacturing process or site of manufacture of excipients derived from Category IC ruminant tissues (including from animal to plant or non-animal source).

Requires update to ARTG data: Formulation.



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 product must not be administered by the parenteral, ophthalmic or intra-tracheal routes.
- The change must be from a ruminant-derived source to a plant or other non-animal source.
- No changes to the specifications of the excipients are permitted, except for the changes allowed within the [changes to excipients](#) section.

Data requirements

You must submit:

- Details of the excipients and the proposed changes.
- Where relevant, CEP issued by the EDQM to the manufacturer of the excipient.
- A declaration that the Category IC material has been self-assessed and complies with the TGA's requirements regarding Transmissible Spongiform Encephalopathies (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.

ESAM: Excipient specification - change to assay method

Changes to a method used for assaying an excipient.

Conditions

- The proposed method must either:
 - improve at least one of precision, accuracy or specificity without a reduction in the other parameters or
 - the proposed method must improve accuracy or specificity with reduced precision provided precision remains within the specified limits.

Data requirements

You must submit:

- Details of the new assay method.

You must generate the following data:

- Appropriate validation data for the proposed method.

ESIP: Excipient specification - change from an in-house to a pharmacopoeial test method

Changes to the specifications to ensure that the excipient complies with the requirements of a default standard (i.e. a monograph in the BP, USP-NF or EP), where previously no default standard applied.

Conditions

- Change or addition must only be to test methods for physicochemical parameters (e.g. pH, colour, particle size, particulate matter, density, specific gravity, optical rotation, osmolality, osmolarity and viscosity).
- The change must not result from an altered method of manufacture that changes the material's quality characteristics (such as micronisation).
- Applied limits must be based on batch analytical data, and comply with any applicable official standard (TGO or default standard) or [adopted guidelines](#).
- Any tests that are performed in addition to those of the pharmacopoeial monograph or TGO for critical parameters (e.g. particle size, pH, viscosity) must continue to be performed.

Data requirements

You must submit:

- The revised set of specifications for the excipient.
- A summary description of the change and details of the new method.

You must generate the following data:

- Validation data for the method(s), as required.
- Equivalency of the current and pharmacopoeial test method(s) must be established by testing of three batches using the current and proposed methods.

ESNL: Excipient specification - narrowing of limits

Revision of the approved specifications for testing of excipients, to make the limits applied to test results more stringent.

Conditions

- The proposed limits must be consistent with any applicable official standard (TGO or default standard) or [adopted guidelines](#).

Data requirements

You must submit:

- A statement of the current and proposed limits.
- The revised set of specifications for the excipient.

ESNT: Excipient specification - new test and limit

Addition of a new test and associated limits to the approved specifications for an excipient.

Conditions

- The change must not result from an altered method of manufacture that changes the material's quality characteristics (such as micronisation).
- Applied limits must be based on batch analytical data, and comply with any applicable official standard (TGO or default standard) or [adopted guidelines](#).

Data requirements

You must submit:

- Details of the new test and limit, including the test method.
- The revised set of specifications for the excipient.

You must generate the following data:

- Appropriate validation data for the proposed method.

ESPT: Excipient specification - changes resulting from pharmacopoeial or TGO requirements

Changes to the specifications for an excipient as a result of amendments to requirements in a default standard (i.e. monograph in BP, USP-NF or EP), or relevant requirements in an applicable standard made by the Minister under section 10 of the [Act](#).

Conditions

- The excipient must be tested to the existing pharmacopoeial or TGO requirements.
- Any tests that are performed in addition to those of the pharmacopoeial monograph or TGO must continue to be performed.
- The new pharmacopoeial monograph or TGO must be applicable to the excipient.

Data requirements

You must submit:

- Details of the proposed change.
- The revised set of specifications for the excipient.

1.6.3 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.

ESCS: Excipient specification – changes to the specifications of the excipients, raw materials and starting materials

Any proposed changes to the specifications of the excipients, raw materials and starting materials can be submitted as part of this Category 3 variation type.



This type of change includes replacement of one type of starch (for example, wheat starch) with another type in a formulation, or changing the grade of an excipient, with no change in quantity in the formulation.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- A copy of the revised specifications.
- Justification for any new or changed limits or test methods.
- Validation of any changed test procedures for critical tests.
- Certificates of analysis for at least one representative batch of the excipient that demonstrates the manufacturer's ability to meet the revised specifications.

- Where necessary (for example, when changing the grade of excipient or changing the type of starch used in a product), relevant validation data, such as comparative dissolution profiles and comparative batch data, that support the changed excipient.

EMPC: Excipients of animal origin – change to source

Any proposed changes to the source of excipients or animal origin can be submitted as part of this Category 3 variation type.

Requires update to ARTG data: Formulation.



Refer to [Guidance 10: Adventitious agent safety of medicines](#), for additional details on requirements for ingredients of human or animal origin.

Conditions

- Data is submitted as described below.

Data requirements

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 A or B tissues from TSE-relevant ruminant species (see the TGA's [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.

EMPM: Excipients of animal origin – change to method of manufacture

Any proposed changes to the method of manufacture of excipients of animal origin can be submitted as part of this Category 3 variation type.



Refer to [Guidance 10: Adventitious agent safety of medicines](#), for additional details on requirements for ingredients of human or animal origin.

Conditions

- Data is submitted as described below.

Data requirements

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 A or B tissues from TSE-relevant ruminant species (see the TGA's [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.

1.7 Container/closure system changes

1.7.1 Changes that do not require reporting to the TGA

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

Non-sterile container - changes to the supplier or manufacturer if same material and specifications

You do not need to notify the TGA if you are making a variation that changes the supplier or manufacturer of non-sterile containers or container components.

Conditions

- The same material type and specifications must be retained.

1.7.2 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 [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#) for further information.

CACI: Correct an ARTG entry - container information

Requires update to ARTG data: Container & Shelf Life.

Conditions

- Data is submitted as described below.

Data requirements

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.

1.7.3 Notifications

These variations fall under s. 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.

CCCA: Container/closure - change to components

Changes to outer packaging or components of the container that are not in direct contact with the drug product.



For sterile products, the container components that are being changed are not required to be sterile.

Conditions

- The change is restricted to one or more of the following:
 - a change to, or addition or removal of, the outer carton or other outer primary pack (including changes to size, shape, colour or material thickness); and/or
 - a change to, or addition or removal of, components of the container that are not in direct contact with the product (for example, tamper-evident seal, aluminium flip-off crimps on injection vials, plastic dust-cover disc/top/cap); and/or
 - the inclusion or removal of inert wadding from bottles and other containers containing solid dosage forms; and/or
 - the inclusion of a desiccant in containers of solid dosage forms; and/or
 - the inclusion of, or change to, an outer overwrap designed to prevent ingress or egress of moisture, solvent or gases from a container (including changes to size, shape or colour, or increased material thickness).
- Other than inert wadding and desiccant, the components must not be in direct contact with the product.
- The label of any outer carton or other primary pack that is added or changed must either be identical to the container label or be changed as permitted under:
 - [Changes to product labels](#) that are notifications and/or
 - Changes that do not require TGA prior approval.
- Where an existing carton or primary pack is removed, the container label must either remain unchanged or be changed as permitted under:
 - [Changes to product labels](#) that are notifications and/or
 - Changes that do not require TGA prior approval and must continue to meet all requirements of the TGO that relates to labels.
- No change can be made to the product's shelf life or storage conditions as a notification. For self-assessable (SAR) changes to the shelf life or storage conditions see:
 - [DSLE: Shelf life - Extension according to an approved stability-testing protocol](#) and
 - [DSL D: Shelf life - Decrease and/or more restrictive storage conditions](#).

- The TGA must be notified as a priority if the results of supporting stability data fail to meet the specifications. The product in the new container system may be withdrawn from the market at the TGA's discretion.

Data requirements

You must submit:

- Details of the change(s).
- Where a desiccant is included in a container, an assurance that the desiccant is used to improve the existing acceptable stability profile of the product and is not used to overcome stability problems in the existing container.
- Where a desiccant is included in a container, information on the nature of the desiccant, as well as information showing that the desiccant is readily distinguishable from the product, and is appropriately labelled and identified as a desiccant.
- If an overwrap is introduced, the rationale for its inclusion, and details of the material of the overwrap and specification.

You must generate the following data:

- Where applicable, comparative data to demonstrate the removal of inert wadding has not adversely affected the product's friability and other physical attributes during normal transport.
- Where an overwrap is introduced or changed, a stability study to verify the product shelf life of the product with the overwrap must have commenced at the time of the notification on at least one production-scale batch of the product, and should continue on the second and third batches as they are manufactured.

CCSS: Container/closure - change to size and shape for non-sterile dosage forms

Changes to the size and shape of the container or closure system used for drug products that are non-sterile dosage forms.

Conditions

- The change must not result in a change to the container type.
- If the container is a blister pack or strip pack, the change in size or shape must not result in an increase in the headspace volume of the blister-pack or strip-pack pocket.
- If the container is a reclosable package, there must not be an increase in the headspace of the container.
- The material and thickness of the container/closure system must be either unchanged or changed in a manner permitted under variation types:
 - [CMIT: Container/closure material - increase in thickness for non-sterile solid, semi-solid, semi-liquid or liquid dosage forms](#) and/or
 - [CMDT: Container/closure material - decrease in thickness for blister packs, strip packs and sachets for non-sterile solid or semi-solid dosage forms.](#)
- No change can be made to the product's shelf life or storage conditions as a notification. For self-assessable (SAR) changes to the shelf life or storage conditions see:

- [DSLE: Shelf life - Extension according to an approved stability-testing protocol](#) and
- [DSL D: Shelf life - Decrease and/or more restrictive storage conditions.](#)
- No change can be made to the quantity of products in the new container/closure system.
- The TGA must be notified as a priority if the results of supporting stability data fail to meet the specifications. The product in the new container system may be withdrawn from the market at the TGA's discretion.

Data requirements

You must submit:

- Details of the new container/closure system, with specifications, if relevant.
- If the closure is a child-resistant cap, or implied by its presentation and construction to be one, a declaration that the reclosable package meets all of the requirements of the current TGO on child-resistant packaging. The declaration must state, in particular, 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.

You must generate the following data:

- If the container is a reclosable package and is child-resistant (or is implied by its presentation to be a child-resistant package), data must have been generated to demonstrate that the child-resistant properties of the package and operation of the closure have not been adversely affected by the change in size and shape.
- For solid oral dosage forms, comparative moisture permeability (water-vapour transmission) data must have been generated on the new and current container systems using the current edition of the USP test for containers—permeation (multi-unit or single-unit containers, as appropriate), and the results must show either equivalent or better moisture protection.
- A stability study using the new container/closure system to verify the product shelf life must have been initiated on at least one production-scale batch of the product (with at least two more production batches to be similarly tested).

CCST: Container/closure - changes to specification and test methods

Changes to the specifications for the container or closure system of the final drug product, to include new tests, make specified limits more stringent, delete a test procedure or make minor changes to test methods.

Conditions

- There must be no change to container dimensions or components, other than those specified in:
 - [CCSS: Container/closure - change to size and shape for non-sterile dosage forms](#) and/or
 - [CCCA: Container/closure - change to components.](#)
- The limits applied must be based on batch analytical data, and comply with any applicable official standard or relevant guidelines adopted by the TGA.
- The packaging components must remain compliant with pharmacopoeial requirements and food standards.
- The change does not result from unexpected events arising during manufacture.

Data requirements

You must submit:

- Updated specifications and test methods.

You must generate the following data:

- Validation data for the proposed method demonstrating that the updated test procedure is at least equivalent to the former test procedure.

CMDT: Container/closure material - decrease in thickness for blister packs, strip packs and sachets for non-sterile solid or semi-solid dosage forms

Decrease in the thickness of aluminium foil, or laminate material used in laminated aluminium foil, for blister packs, strip packs and sachets containing non-sterile solid or semi-solid drug products.

Conditions

- The product must be a non-sterile dosage form.
- The material that is decreased in thickness must be either the aluminium foil or, in the case of a laminated aluminium foil, the aluminium foil itself or any non-aluminium polymeric material laminated to it.
- The new aluminium foil thickness or the aluminium component of the laminated foil must be at least 20 µm.
- The container/closure material must be unchanged.
- No change should be made to the product's shelf life or storage conditions. See [self-assessable changes to the shelf life or storage conditions](#).
- The TGA must be notified as a priority if the results of supporting stability data fail to meet the specifications. The product in the new container system may be withdrawn from the market at the TGA's discretion.

Data requirements

You must submit:

- Details of the change in thickness of the container material, with specifications, if relevant.

You must generate the following data:

- A stability study using the new container/closure system to verify the product shelf life must have been initiated on at least one production-scale batch of the product (with at least two more production batches to be similarly tested).

CMIT: Container/closure material - increase in thickness for non-sterile solid, semi-solid, semi-liquid or liquid dosage forms

Increase in the thickness of the material used for the container or closure system of non-sterile solid, semi-solid, semi-liquid or liquid drug products.

Conditions

- The container/closure material must be unchanged.
- No change can be made to the product's shelf life or storage conditions as a notification. For self-assessable (SAR) changes to the shelf life or storage conditions see:
 - [DSLE: Shelf life - Extension according to an approved stability-testing protocol](#) and
 - [DSL D: Shelf life - Decrease and/or more restrictive storage conditions](#).
- The TGA must be notified as a priority if the results of supporting stability data fail to meet the specifications. The product in the new container system may be withdrawn from the market at the TGA's discretion.

Data requirements

You must submit:

- Details of the change in thickness of the container/closure material, with specifications, if relevant.

You must generate the following data:

- A stability study using the new container/closure system to verify the product shelf life must have been initiated on at least one production-scale batch of the product (with at least two more production batches to be similarly tested).

1.7.4 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.

CMBP: Container/closure material - changes to material used for blister packs, strip packs and sachets of non-sterile dosage forms

Changes to the material of a container/closure system - blister packs, strip packs and sachets.

Requires update to ARTG data: Container & Shelf Life.

Conditions

- The product should be a non-sterile solid (such as tablets or capsules) or semi-solid dosage form (such as moulded suppositories and pessaries) in blister packs, strip packs or sachets.
- The plastic component of the container may be changed from:
 - PVC to PVC/polyvinylidene chloride (PVDC) or PVC/polychlorotrifluoroethylene (PCTFE) or PVC/PVDC/PE; or
 - PVC/PVDC to PVC/PCTFE or PVC/PVDC/PE; or
 - polypropylene to PVC/PVDC or PVC/PVDC/PE; or

- PVC to polypropylene; or
- any type of plastic material to double aluminium foil blister packs (cold-formed laminated aluminium/aluminium blister packs) or double aluminium foil strip packs.
- Any new plastic material used should meet current pharmacopoeial (BP/Ph. Eur./USP) requirements for plastic materials used for the manufacture of containers.
- Comparative moisture permeability (water-vapour transmission) data should have been generated on the new and current blister-pack or strip-pack system using the current edition of the USP test for containers—permeation (single-unit containers and unit-dose containers), and the results should show either equivalent or better moisture protection.
- A stability study using the new container system to verify the product shelf life should have begun on at least one production-scale batch of the product, and should begin on the second and third batches as they are manufactured.
- If the results of the stability study fail to meet the specifications, the TGA should be notified as a priority, and the product in the new container system may be withdrawn from the market at the TGA's discretion.
- No change should be made to the product's shelf life or storage conditions. See subsection [Product shelf life or storage conditions changes](#) for self-assessable changes to the shelf life or storage conditions.

Data requirements

You must submit:

- Details of the new container material, including specifications, if relevant.
- Where the proposed change requires an update to the PI, details of the amended PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

CMBT: Container/closure material - changes to material used for bottles, jars and tubes of non-sterile dosage forms

Changes to the material of a container/closure system - bottles, jars and tubes.

Requires update to ARTG data: Container & Shelf Life.

Conditions

- The product should be a non-sterile solid dosage form (for example, tablets, capsules, compressed pessaries and suppositories) or a non-sterile semi-solid, semi-liquid or liquid (for example, ointment, gel, cream, lotion, oral solution or suspension).
- The material of which the container/closure system (including a reclosable package) is made may be changed from:
 - polystyrene to polyvinyl chloride (PVC), polyethylene (PE), polypropylene or glass; or
 - PVC to PE, polypropylene or glass; or
 - PE to glass or polypropylene with a density of at least 0.89; or
 - PE of one density to PE of a higher density; or

- glass, metal or PE with a density of at least 0.95 to polypropylene with a density of at least 0.89.
- Any new plastic material used should meet current default standard (BP/Ph. Eur./USP) requirements for materials used for the manufacture of containers, as well as any other guidelines adopted by the TGA.
- If the product is a semi-solid, a semi-liquid or a liquid, it should be water-based and should not contain organic solvent.
- If the container and/or closure system is a child-resistant package or is implied by its presentation to be a child-resistant package, data should have been generated to demonstrate that the child-resistant properties of the package and operation of the closure have not been adversely affected by the change in material, in accordance with the current TGO on child-resistant packaging of medicines.
- If the product is a solid dosage form, comparative moisture permeability (water-vapour transmission) data should have been generated on the new and current container/closure systems using the current edition of the USP test for containers—permeation (multi-unit containers), and the results should show either equivalent or better moisture protection.
- A stability study using the new container/closure system to verify the product's shelf life should have started on at least one production-scale batch of the product, and should begin on the second and third batches as they are produced.
- If the results of the stability study fail to meet the specifications, the TGA should be notified as a priority after the failure is detected, and the product in the new container/closure system may be withdrawn from the market at the TGA's discretion.
- No change should be made to the product's shelf life or storage conditions. See subsection 'Product shelf life or storage conditions changes' for self-assessable changes to the shelf life or storage conditions.

Data requirements

You must submit:

- Details of the new container/closure system, including any new material used and the material or container specifications (where relevant).
- If the closure is a child-resistant cap (or is implied by its presentation and construction to be a child-resistant cap), a declaration that the reclosable package meets all of the requirements of the current TGO on child-resistant packaging. The declaration should state, in particular, 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.
- Where the proposed change requires an update to the PI, details of the amended PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

1.7.5 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.

CCSC: Container/closure system - changes to container components and/or dimensions

Any proposed changes to the components or dimensions of the container or closure system (or specifications for the container or closure system) can be submitted as part of this Category 3 variation type. This includes container shape, size and material, as well as any measuring or delivery system included in the pack, but excludes container type. For changes to container type see [PCCT: Packaging - changes to container type – New AUST R number](#).

Requires update to ARTG data: Container & Shelf Life.

Note: If your entry allows the medicine container to be made of alternative materials (for example glass and plastic ampoules; PVCD/ aluminium and PVC/ aluminium blisters) you will need to include separate Container & Shelf Life details for each container material. Include these details in both the cover letter and the comments field of the application.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- Description and specifications of container/closure system and materials.
- If relevant, biomaterial safety evidence that any new polymeric or rubber container/closure materials that are in contact with the product are free from 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 accordance with GMP requirements. Comparative moisture permeability data of the current and proposed container/closure system may be required.
- Validation data on the changed measuring/delivery system in the pack, if relevant.
- 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 reclosable 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.
- For sterile products, sterile manufacture information and sterility testing data, as appropriate, including information such as validation of aseptic processes 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 requires an update to the PI, details of the amended PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).
- For non-sterile multi-dose oral liquid or suspension products, preservative efficacy test data.

1.7.6 Category 3 requests - Data evaluation required under s. 23 (separate and distinct good) – New AUST R number

These variations fall under s. 23 of the [Therapeutic Goods Act 1989](#) and require the submission of data for evaluation.

PCCT: Packaging - changes to container type – New AUST R number

Any proposed changes to the container type can be submitted as part of this Category 3 variation type.

Requires update to ARTG data: Container & Shelf Life.



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

- Data is submitted as described below.

Data requirements

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 must be provided. Where the proposed change would involve amendment of a PI, a marked-up copy should also be provided, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

Associated changes

You may need to update other information about your medicine as a result of the changes to the container. Associated variation types that you can include with PCCT are:

- [ZFNM: ARTG data – Manufacturer changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNN: ARTG data – Good name changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNO: Other consequential changes to the dossier associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNP: ARTG data – Pack size and poison schedule changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNS: ARTG data – Sterility changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)
- [ZFNV: ARTG data – Visual identification changes associated with DFNA/PFNA or PCCT – For the new AUST R number](#)

1.8 Pack size changes

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 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.



1.8.1 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 [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#) for further information.

CAPS: Correct an ARTG entry – pack size & poison schedule

Requires update to ARTG data: Pack Size & Poison Schedule.

Conditions

- Data is submitted as described below.

Data requirements

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.

1.8.2 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.

PSAC: Pack size - addition or change to pack size excluding volume of fill of injections or other sterile preparations

Requires update to ARTG data: Pack Size & Poison Schedule.

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 a Pharmaceutical Benefits Advisory Committee recommendation (including a larger pack size); or
 - to introduce a smaller pack size; or
 - to delete 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 products or other changes allowed under section K, below, and/or Part 6 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 other sections of this document.

Data requirements

You must submit:

- Relevant details regarding the change in pack size.
- A copy of the label for the new pack size.
- Where the proposed change requires an update to the PI, details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

1.8.3 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.

PSCA: Pack size - change to, or addition of, pack size

Any proposed changes to the pack size can be submitted as part of this Category 3 variation type.

Requires update to ARTG data: Pack Size & Poison Schedule.

Conditions

- Data is submitted as described below.

Data requirements

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 [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

1.9 Product shelf life or storage conditions changes**Pre-approved stability-testing protocols**

Stability-testing protocols can be approved in advance, so that the shelf life of a product can be extended through self-assessment. Such protocols may be submitted with the application for registration of a product or with an application to vary the registration. When a stability-testing protocol is submitted, at least 12 months of stability data should be available for the product (or a closely related formulation) in the marketed container or a less protective container.



- Any stability-testing protocol proposed for this purpose should include:
- Information on the number of batches to be tested (minimum of three production-scale batches) and container/closure to be used
- A statement of the proposed tests and methods

- A matrix indicating the time points at which each of the tests will be conducted, including storage conditions and duration
- Acceptance limits for the results for each test. Some test limits (particularly those with quantitative results, such as assay, dissolution/disintegration, and impurities/degradation products) should be more stringent than the approved expiry limits, but not necessarily as stringent as the release limits.

1.9.1 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 [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#) for further information.

CASL: Correct an ARTG entry - shelf life / storage condition

Requires update to ARTG data: Container & Shelf Life.

Conditions

- Data is submitted as described below.

Data requirements

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.

1.9.2 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.

DSL: Shelf life - decrease and/or more restrictive storage conditions

If changes to shelf life or storage conditions are requested because of a problem with stability, data are required for evaluation, and the variation is not self-assessable.

Requires update to ARTG data: Container & Shelf Life.

Conditions

- Adequate stability data for at least three production-scale batches of the product should have been generated to support the new shelf life and/or storage conditions.
- Where relevant, product labels and the PI should be changed to reflect the new storage conditions and/or shelf life.

Data requirements

You must submit:

- Reasons for the change.
- Details of the new shelf life and/or storage conditions.
- A copy of the revised product labels.
- Where the proposed change requires an update to the PI, details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

DSLE: Shelf life - extension according to an approved stability-testing protocol

Requires update to ARTG data: Container & Shelf Life.

Conditions

- This does not apply to the in-use shelf life for multi-dose products.
- A stability-testing protocol should have been previously approved by the TGA through self-assessment, explicitly for the purpose of extending the shelf life. See the definition of a [pre-approved stability-testing protocol](#) above.
- At least three production-scale batches of the product should have been tested in accordance with the approved stability-testing protocol.
- The extended shelf life should not be longer than the time for which stability data meeting the approved protocol requirements are available, and should not be longer than five years.
- The extended shelf life should not be based on extrapolation of the stability data generated according to the approved protocol.

Data requirements

You must submit:

- Evidence that the TGA has approved the protocol for the purpose of shelf life extension through self-assessment. See the definition of a [pre-approved stability-testing protocol](#) above.
- The new shelf life and storage conditions.
- Where the proposed change requires an update to the PI, details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

1.9.3 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.

DSLCL: Shelf life - changes to the shelf life or storage conditions of the drug product.

Any proposed changes to the shelf life or storage conditions of the drug product can be submitted as part of this Category 3 variation type.

Requires update to ARTG data: Container & Shelf Life.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- Stability data generated according to ICH guidelines on at least three production-scale batches to support the change. Data from fewer batches or pilot-scale batches may be acceptable, if justified.
- Revised labelling, if the storage conditions are to be changed.
- Where the proposed change requires an update to the PI, details of the amended PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).
- For increases in shelf life of multi-dose liquid products, preservative efficacy data, as specified in [TGO 100](#) (see [Guidance 17: Microbial quality of prescription and over-the-counter medicines](#)).

1.10 Product information (PI) changes: Quality aspects, corrections and self-assessable requests (SARs)

The changes listed here are to the quality aspects of the product information, corrections to the PI and SARs. For safety related requests, minor editorial changes and extension of indications see [Part 2: Product information \(PI\) changes](#).

Consequential changes to the product information



Changes to the PI that are a consequence of a quality change **do not** require a separate variation type to be selected. These PI changes should be submitted with the quality change request. See Consequential changes to the product information that result from variations to an ARTG entry in [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

A single PI often refers to multiple ARTG entries (products). If the affected PI refers to additional ARTG entries that are not selected in Variation e-form then these additional ARTG entries should be listed in the application cover letter and comments field of the Variation e-form. A statement should be included requesting that the PI for these additional products is also varied.

1.10.1 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 [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; 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.

Data requirements

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.

1.10.2 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.

Data requirements

You must submit:

- Details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; 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.

Data requirements

You must submit:

- Details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; 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.

Data requirements

You must submit:

- Details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; 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.

Data requirements

You must submit:

- Details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; 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.

Data requirements

You must submit:

- Details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; 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.

Data requirements

You must submit:

- Details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; 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.

1.10.3 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

Proposed quality-related changes to the ARTG entry resulting in changes to the PI that are not described above may be submitted as this variation type. However, changes to the PI that are a consequence of a quality change do not require a separate variation type to be selected. These PI changes should be submitted with the quality change request. See Consequential changes to the product information that result from variations to an ARTG entry and Multiple related changes in [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

Note that safety-related changes to the PI must be separately submitted as a SRR.

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- A description of the proposed changes to the PI.
- Details of changes to the PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).
- Relevant technical data to support the proposed change(s).

1.11 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.



Multiple related and unrelated changes to the label

Multiple changes to the label may not require the selection of multiple variation types. For information and an example on submitting multiple unrelated changes to medicine labels see [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

Consequential changes to the label (changes to the label that are a consequence of a quality change) **do not** require a separate variation type to be selected. These label changes should be submitted with the quality change request. See Multiple related changes with an example in the process guidance.

1.11.1 Changes that do not require reporting to the TGA

These changes can be implemented without reporting to 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 (e.g. new formulation)
- 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 or serialisation pharmacode (e.g. EU pharmacode)
- 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
- change to the prefix used for batch and/or expiry details
- change in location of the prefix used for batch and/or expiry details.

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 ™.
- The prefixes must be one of those stated in Section 6 of the Therapeutic Goods Order No. 91. The batch number of the medicine must be preceded by the batch number prefix and the expiry date of the medicine is preceded by the expiry date prefix.

1.11.2 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.

LOCI: Label - consequential change resulting from a change approved under subsection 9D(3) or conditions imposed under subsection 28(3)

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.

Data requirements

- 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.
- Evidence of the approval of the previous change (such as a TGA submission number).

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.

Data requirements

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.

Data requirements

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.

Data requirements

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.

Data requirements

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.

Data requirements

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.

Data requirements

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

Data requirements

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 - adding information either on label or as insert advising of patient support program (PSP)

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.
- All references to Patient Support Programs (PSPs) must have the following disclaimer prominently stated - "Patient Support Program complies with the Medicines Australia code of conduct, however it is not authorised or approved by the Therapeutic Goods Administration".

Data requirements

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.

LPQR: Label - inclusion of QR code

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 link must be for an Australian owned and managed company and must not include any element of a promotional nature.

Data requirements

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.

LPRP: Label - removal of phrases such as 'New formulation', 'New appearance' after a period of time.**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.
- There must be a sufficient period of time that has elapsed to advise the market of the new product.

Data requirements

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.

LQAE: 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.

Data requirements

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.

LQAT: 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.

Data requirements

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.

LQHI: 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.

Data requirements

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.

LQRT: 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.

Data requirements

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).

LWAH: 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 (e.g. 'Not for injection', 'For external use only' and 'Not for oral use').

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.

Data requirements

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.

LWSR: 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.

Data requirements

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).

1.11.3 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.

Data requirements

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

Proposed changes as a result of approved corrections can be submitted as this variation type. However, for changes to labels as a consequence of another change that are requested at the same time, a separate variation type is not required. For further information and an example see [Multiple related changes in Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

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 amendments are due to implementation of corrections that have been approved under s. 9D(1) of the [Therapeutic Goods Act 1989](#).

Data requirements

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.

Data requirements

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.

Data requirements

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.

Data requirements

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 approval from the TGA

Refer to this guidance for the types of variations included within 'Changes that do not require prior approval' from the TGA. For information about reporting on changes that do not require prior TGA approval see [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

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 can apply to manufacturers who are also product sponsors.
- The change to the address is allowable provided the actual site location does not change.

Data requirements

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

Proposed changes as a result of approved SARs can be submitted as this variation type. However, for changes to labels as a consequence of another change that are requested at the same time, a separate variation type is not required. For further information and an example see Multiple related changes in [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

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.

Data requirements

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.

Data requirements

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

- All changes to the label must be identified in the request.
- The changes must ensure continued compliance with the relevant TGO pertaining to labels.
- The change results from a requirement by other relevant Australian legislation.

Data requirements

You must submit:

- Copies of the existing labels and final copies or mock-ups of the amended labels, including any logos, designs or graphics. The copy should preferably be of actual size and should indicate the colours to be used. If there are multiple pack sizes or strengths, one representative label or copy will be sufficient, provided that the only difference between the labels is the pack size or strength, unless this would contravene the strength differentiation requirement.

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.

Data requirements

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.

Data requirements

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.

Data requirements

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.

1.11.4 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.

LCDE: Label changes - any changes requiring evaluation

Any proposed changes to the label can be submitted as part of this Category 3 variation type.

Conditions

- Data is submitted as described below.

Data requirements

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.

1.11.5 Category 3 requests - Data evaluation required under s. 23 (separate and distinct good) – Retaining AUST R number

These variations fall under s. 23 of the [Therapeutic Goods Act 1989](#) and require the submission of data for evaluation.

DTTR: Trade name replacement – Retaining AUST R number

Replacement of trade name.

Requires update to ARTG data: Good 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.

Data requirements

You must submit:

- Proposed replacement trade name.
- Revised labels.

- 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 must be provided. Where the proposed change would involve approval of a new PI, a marked-up copy should also be provided, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).
- If submitting the application on behalf of another sponsor and/or using your name, contact details or livery on the labels, a letter of authorisation from the sponsor authorising you to submit the application and permission for your contact details and livery to be used on the labels.

Associated changes

You may need to update other information about your medicine as a result of the changes to the trade name. Associated variation types that you can include with DTTR are:

- [ZFCR: ARTG data – Container and shelf life changes associated with DFCE/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRM: ARTG data – Manufacturer changes associated with DFCE/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRO: Other consequential changes to the dossier associated with DFCE/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRP: ARTG data – Pack size and poison schedule changes associated with DFCE/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRS: ARTG data – Sterility changes associated with DFCE/PFCF or DTTR – Retaining AUST R number](#)
- [ZFRV: ARTG data - Visual identification changes associated with a result of DFCE/PFCF or DTTR – Retaining AUST R number.](#)

1.12 Other changes

1.12.1 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 [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#) for further information.

CADF: Correct an ARTG entry - dosage form

Requires update to ARTG data: Dosage Form.

Conditions

- Data is submitted as described below.

Data requirements

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

Requires update to ARTG data: Good Name.

Conditions

- Data is submitted as described below.

Data requirements

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

Requires update to ARTG data: Indications.

Conditions

- Data is submitted as described below.

Data requirements

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

Requires update to ARTG data: ATC Nordic Codes.

Conditions

- Data is submitted as described below.

Data requirements

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***

- Data is submitted as described below.

Data requirements

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

Requires update to ARTG data: Route of Administration.

Conditions

- Data is submitted as described below.

Data requirements

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

Requires update to ARTG data: Sterility Information.

Conditions

- Data is submitted as described below.

Data requirements

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

Requires update to ARTG data: Visual Identification.

Conditions

- Data is submitted as described below.

Data requirements

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.

1.12.2 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.

OCPS: medicines and poisons - change in scheduling

Requires update to ARTG data: Pack Size & Poison Schedule.



Changes to medicines and poisons scheduling

Any changes to the [Standard for the Uniform Scheduling of Medicines and Poisons](#) signal heading and cautionary statements are matters for the states and territories, and therefore should be handled through state and territory authorities.

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 [Australian Regulatory Guidelines for Over-the-Counter Medicines](#), where appropriate.

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](#)).

Data requirements

You must submit:

- Relevant evidence of the change, such as a copy of the final [Advisory Committee on Medicines Scheduling \(ACMS\)](#) decision.

- A copy of the revised label.
- A clean and marked-up copy of the proposed amended PI, as outlined in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

SARO: Other self-assessable changes - an application using this type must include written advice from the TGA

Conditions

- Data is submitted as described below.

Data requirements

You must submit:

- Written advice from the TGA advising the use of this variation type.
- Details of the proposed changes and appropriate supporting data relevant to the change(s) concerned.
- Details of the variation should be described in both the cover letter and in the comments field of the e-form.

1.12.3 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.

OCQD: Other quality changes that do not create a separate and distinct good

This can include quality-related changes that do not create a separate and distinct good that are not covered by a variation type described in this document.

Conditions

- The variation does not create a separate and distinct good.

Data requirements

You must submit:

- Details of the proposed changes and appropriate supporting data relevant to the change(s) concerned.
- Details of the variation should be described in both the cover letter and in the comments field of the Variation e-form.

1.13 Associated changes

When requesting a change that will result in a new and distinct good, there may be situations where your variation requires multiple PAR fields to be updated. For example, varying the formulation of your product may result in the need to update the visual identification information.

To prevent the creation of unnecessary separate submissions you can use the 'Associated changes.' These variation types are listed here. They can only be selected in combination with the variation type specified in the conditions. Variations that can be requested as 'Associated changes' must be described in other parts of this guidance and must not require evaluation of clinical or bioequivalence data. The conditions stated in other parts of the guidance for related variation types would also apply to the associated variation types.

See also:

- Associated changes in [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).
- [Associated changes to product information \(PI\)](#).

1.13.1 Changes associated with DFCI and DFFC

ZFSM: ARTG data - Manufacturer changes associated with DFCI or DFFC

Change to data within ARTG Manufacturers associated with a change to an inked imprint or to a colouring agent, flavour or fragrance.

Requires update to ARTG data: Manufacturers.

Conditions

- This variation type can only be selected in combination with either:
 - [DFCI: Formulation - addition or deletion of, or variation to, an inked imprint](#)
 - [DFFC: Formulation - change relating to colouring agent, flavour or fragrance](#).
- This change that is associated with DFCI or DFFC is not a category 3 change requiring the submission of data for evaluation. If this associated change is a category 3 change, select a category 3 formulation variation type first, then an associated change. See [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#) and [DFNA: Formulation changes \(CE\) – New AUST R number](#).
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Manufacturers variation types.

ZFSV: ARTG data - Visual identification changes associated with DFCI or DFFC

Change to data within ARTG Visual Identification as a consequence of a change to an inked imprint or to a colouring agent, flavour or fragrance.

Requires update to ARTG data: Visual Identification.

Conditions

- This variation type can only be selected in combination with either:
 - [DFCI: Formulation - addition or deletion of, or variation to, an inked imprint](#)
 - [DFFC: Formulation - change relating to colouring agent, flavour or fragrance.](#)
- This change that is associated with DFCI or DFFC is not a category 3 change requiring the submission of data for evaluation. If this associated change is a category 3 change, select a category 3 formulation variation type first, then an associated change. See [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#) and [DFNA: Formulation changes \(CE\) – New AUST R number](#).
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Visual Identification variation types. For example the new product description.

1.13.2 Changes associated with DFCF and DTTR

ZFRC: ARTG data – Container and shelf life changes associated with DFCF/PFCF or DTTR – Retaining AUST R number

Change to data within ARTG Container & Shelf Life associated with a s.23 Category 3 change to formulation or trade name.

Requires update to ARTG data: Container & Shelf Life.

Conditions

- This variation type can only be selected in combination with:
 - [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#)
 - [DTTR: Trade name replacement – Retaining AUST R number.](#)
- The change is only to container material or shelf life.
- This change that is associated with DFCF or DTTR is not a change that requires a new AUST R number. If this associated change requires a new AUST R number use [DFNA: Formulation changes \(CE\) – New AUST R number](#) then [changes associated with DFNA and PCCT](#).
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate stability data as described in relevant Container & Shelf Life variation types.

ZFRM: ARTG data – Manufacturer changes associated with DFCF/PFCF or DTTR – Retaining AUST R number

Change to data within ARTG Manufacturers associated with a s.23 Category 3 change to formulation or trade name.

Requires update to ARTG data: Manufacturers.

Conditions

- This variation type can only be selected in combination with:
 - [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#)
 - [DTTR: Trade name replacement – Retaining AUST R number.](#)
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Manufacturers variation types.

ZFRN: ARTG data – Good name changes associated with DFCF/PFCF – Retaining AUST R number

Change to data within ARTG Good Name associated with a s.23 Category 3 change to formulation.

Requires update to ARTG data: Good 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

- This variation type can only be selected in combination with:
 - [DFCF: Formulation – changes \(CE\) – Retaining AUST R number.](#)
- This change that is associated with DFCF is not a change that requires a new AUST R number. If this associated change requires a new AUST R number use [DFNA: Formulation changes \(CE\) – New AUST R number](#) then [changes associated with DFNA and PCCT.](#)

- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Good Name variation types.

ZFRO: Other consequential changes to the dossier associated with DFCF/PFCF or DTTR – Retaining AUST R number

Change to data within the dossier associated with a s.23 Category 3 change to formulation or trade name.

Conditions

- This variation type can only be selected in combination with:
 - [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#)
 - [DTTR: Trade name replacement – Retaining AUST R number.](#)
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.
- This change does not require an update to ARTG data.

Data requirements

You must submit:

- Appropriate data as described in relevant variation types.

ZFRP: ARTG data – Pack size and poison schedule changes associated with DFCF/PFCF or DTTR – Retaining AUST R number

Change to data within ARTG Pack Size & Poison Schedule associated with a s.23 Category 3 change to formulation or trade name.

Requires update to ARTG data: Pack Size & Poison Schedule.

Conditions

- This variation type can only be selected in combination with:
 - [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#)
 - [DTTR: Trade name replacement – Retaining AUST R number.](#)
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Pack Size & Poison Schedule variation types.

ZFRS: ARTG data – Sterility changes associated with DFCF/PFCF or DTTR – Retaining AUST R number

Change to data within ARTG Sterility associated with a s.23 Category 3 change to formulation or trade name.

Requires update to ARTG data: Sterility.

Conditions

- This variation type can only be selected in combination with:
 - [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#)
 - [DTTR: Trade name replacement – Retaining AUST R number](#).
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Sterility variation types.

ZFRV: ARTG data - Visual identification changes associated with DFCF/PFCF or DTTR – Retaining AUST R number

Change to data within ARTG Visual Identification as a consequence of a s.23 Category 3 change to formulation or trade name.

Requires update to ARTG data: Visual Identification.

Conditions

- This variation type can only be selected in combination with:
 - [DFCF: Formulation – changes \(CE\) – Retaining AUST R number](#)
 - [DTTR: Trade name replacement – Retaining AUST R number](#).
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Visual Identification variation types. For example the new product description.

1.13.3 Changes associated with DFNA and PCCT

ZFNC: ARTG data – Container and shelf life changes associated with DFNA/PFNA – For the new AUST R number

Change to data within ARTG Container & Shelf Life associated with a s.23 Category 3 change to formulation.

Requires update to ARTG data: Container & Shelf Life.

Conditions

- This variation type can only be selected in combination with:
 - [DFNA: Formulation changes \(CE\) – New AUST R number](#).
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate stability data as described in relevant Container & Shelf Life variation types.

ZFNM: ARTG data – Manufacturer changes associated with DFNA/PFNA or PCCT – For the new AUST R number

Change to data within ARTG Manufacturers associated with a s.23 Category 3 change to formulation or container type.

Requires update to ARTG data: Manufacturers.

Conditions

- This variation type can only be selected in combination with:
 - [DFNA: Formulation changes \(CE\) – New AUST R number](#)
 - [PCCT: Packaging - changes to container type – New AUST R number](#).
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Manufacturers variation types.

ZFNN: ARTG data – Good name changes associated with DFNA/PFNA or PCCT – For the new AUST R number

Change to data within ARTG Good Name associated with a s.23 Category 3 change to formulation or container type.

Requires update to ARTG data: Good Name.

Conditions

- This variation type can only be selected in combination with:
 - [DFNA: Formulation changes \(CE\) – New AUST R number](#)
 - [PCCT: Packaging - changes to container type – New AUST R number.](#)
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Good Name variation types.

ZFNO: Other consequential changes to the dossier associated with DFNA/PFNA or PCCT – For the new AUST R number

Change to data within the dossier associated with a s.23 Category 3 change to formulation or container type.

Conditions

- This variation type can only be selected in combination with:
 - [DFNA: Formulation changes \(CE\) – New AUST R number](#)
 - [PCCT: Packaging - changes to container type – New AUST R number.](#)
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.
- This change does not require an update to ARTG data.

Data requirements

You must submit:

- Appropriate data as described in relevant variation types.

ZFNP: ARTG data – Pack size and poison schedule changes associated with DFNA/PFNA or PCCT – For the new AUST R number

Change to data within ARTG Pack Size & Poison Schedule associated with a s.23 Category 3 change to formulation or container type.

Requires update to ARTG data: Pack Size & Poison Schedule.

Conditions

- This variation type can only be selected in combination with:
 - [DFNA: Formulation changes \(CE\) – New AUST R number](#)
 - [PCCT: Packaging - changes to container type – New AUST R number.](#)
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Pack Size & Poison Schedule variation types.

ZFNS: ARTG data – Sterility changes associated with DFNA/PFNA or PCCT – For the new AUST R number

Change to data within ARTG Sterility associated with a s.23 Category 3 change to formulation or container type.

Requires update to ARTG data: Sterility.

Conditions

- This variation type can only be selected in combination with:
 - [DFNA: Formulation changes \(CE\) – New AUST R number](#)
 - [PCCT: Packaging - changes to container type – New AUST R number.](#)
- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Sterility variation types.

ZFNV: ARTG data – Visual identification changes associated with DFNA/PFNA or PCCT – For the new AUST R number

Change to data within ARTG Visual Identification associated with a s.23 Category 3 change to formulation or container type.

Requires update to ARTG data: Visual Identification.

Conditions

- This variation type can only be selected in combination with:
 - [DFNA: Formulation changes \(CE\) – New AUST R number](#)
 - [PCCT: Packaging - changes to container type – New AUST R number.](#)

- This change does not require evaluation of clinical or bioequivalence data and is described in other parts of this guidance. The conditions outlined in the relevant variation type are satisfied.

Data requirements

You must submit:

- Appropriate data as described in relevant Visual Identification variation types. For example the new product description.

2. Product information (PI) changes

The Variation e-form has four category groups which are described in [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#):

- Correct an ARTG entry
- Notification
- Quality information
- Product information (PI).

Part 2 of this guidance describes the changes that can be made within the product information category group. This includes changes to the PI that are minor editorial changes, safety related requests and extension of indications to align with a reference product.

For changes to the quality aspects of the PI, corrections to the PI and self-assessable requests (SARs) related to PI information see [Part 1: Corrections, notifications and quality information changes](#) and [Product information \(PI\) changes: Quality aspects, corrections and self-assessable requests \(SARs\)](#).

2.1 Product information (PI) changes: Minor editorial changes and safety-related requests (SRRs)



All ARTG entries included in the PI document (and therefore will be affected by a change to the PI) should be selected in the Variation e-form when requesting the variation. If an ARTG entry included in the PI document is not selected, a subsequent variation request will be required to be submitted.

For information about selection of ARTG entries for variations that are consequence of a quality change see consequential changes to the product information in [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

2.1.1 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. 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.

Data requirements

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.

2.1.2 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

Requires update to ARTG data: Indications.

Conditions

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

Data requirements

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.
- Revised labels, if applicable.

PIIN: PI - remove an indication - no data

Requires update to ARTG data: Indications.

Conditions

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

Data requirements

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.
- Revised labels, if applicable.

PIOD: PI – make safety related changes with data

Conditions

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

Data requirements

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.
- Revised labels if applicable.

PION: PI - make safety related changes no data

Conditions

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

Data requirements

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.
- Revised labels if applicable.

2.2 Extension of indications

For proposed extension of indications that require evaluation of clinical, pre-clinical or bio-equivalence data, submit an application using the [Prescription Medicines Registration Process](#).

2.2.1 Extension of indications to align with a reference product

These variations fall under s. 23 of the [Therapeutic Goods Act 1989](#). Regulation 16G of the [Therapeutic Goods Regulations 1990](#) must apply, that is, evaluation of clinical, pre-clinical or bio-equivalence data is not required.

PIES: Extension of specific indications to align with a reference product

Proposed extension of indications to align with a reference product where evaluation of clinical, pre-clinical or bio-equivalence data is not required can be submitted as part of this variation type.

Requires update to ARTG data: Indications.



The AUST R number can be retained

Under s. 16(1) of the [Therapeutic Goods Act 1989](#), a change in indication means that the varied 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

- This request is not combined with any other application in the one submission.
- The proposed indication is identical to the approved indication for the reference medicine.
- Bioequivalence to the reference product has previously been demonstrated and evaluated by the TGA.
- There is equivalence for all relevant pharmacokinetic parameters.
 - For different indications, there can be different pharmacokinetic parameters that are relevant to safety and/or efficacy. The pharmacokinetic parameters that we evaluated previously in relation to the reference medicine should still be appropriate and suitable for the new indication. This is because your generic medicine must have the same safety and efficacy properties as the reference medicine (Schedule 9 of the *Therapeutic Goods Regulations 1990*).
 - Examples of pharmacokinetic parameters that are only relevant for some indications:
 - the median Tmax is important for indications that require rapid release from an oral dosage form
 - partial AUC values are sometimes important.
 - For more information see the TGA guidance on [biopharmaceutic studies](#)
- The currently registered strengths are appropriate for the recommended doses for the new indication.
 - Consider the appropriateness of the currently registered strengths of your medicine as they relate to the recommended doses for the new indication.
 - Be careful when using the product information (PI) for the reference medicine to support your extension of indications application. If the range of strengths available for the reference medicine differs from the range of strengths available for your medicine, then you need to consider how strengths relate to dose. For example, if an indication requires a maximum dose of 1 mg and the lowest strength of your medicine is a 5 mg tablet, then the strength of your medicine is inappropriate for the recommended dose for the new indication.
 - If the range of strengths covered by the reference medicine is not the same as for your medicines, consider adding information to the Dosage and administration section of the PI, such as the advice “Use alternative brand for doses that cannot be achieved with [your brand]. Do not name an alternative brand because this is advertising.
- There are no other safety or efficacy issues.

- Consider any other issues related to the need for data to demonstrate that your medicine and the reference medicine have the same safety and efficacy properties.
- For example, for non-absorbable polymers, demonstration of safety and/or efficacy for one indication cannot necessarily be used to support safety and/or efficacy for another indication.
- The intention of this proposed change is to group the new medicine with an already registered prescription medicine.
- Regulation 16G of the *Therapeutic Goods Regulations 1990* applies and this application does not need to be supported by clinical, pre-clinical or bio-equivalence data.

Data requirements

You must submit:

- The trade name, active ingredient(s), ARTG ID and dosage form of the reference medicine and a copy of the reference medicine's product information (PI).
- Justification of why supporting data is not required. Consider all of the following described in the conditions above:
 - identical indication to the reference medicine
 - bioequivalence to the reference medicines
 - equivalence of all relevant pharmacokinetic parameters
 - strength is appropriate for the recommended dose
 - other safety or efficacy issues.
- Justification of decision regarding pack sizes:
 - If you are not applying for additional pack sizes, justify this in relation to the adequacy of current pack sizes to cover the recommended dosage regimen(s) for the new indications.
 - If you are applying for additional pack sizes, justify this in relation to:
 - the inadequacy of current pack sizes to cover the recommended dose regimens for the new indications
 - ability to add pack size without requiring new stability data.
- A clean and marked-up copy of the draft revised PI based on the most recent version of the PI for the existing medicine that has been approved by the TGA. Do not make minor editorial changes to the PI that are not necessary to meet current requirements. The only changes that can be made to the PI are:
 - because of the new indications
 - in order to make the format of the medicine information meet current requirements
 - because of the strengths available.
- A clean and marked up copy of the draft revised CMI.
- Comprehensive table of contents in the CTD.

- Biopharmaceutical studies summary. In module 1.11 provide:
 - a tabulated summary of the pharmacokinetic parameters of the biopharmaceutical studies previously submitted and evaluated by the TGA
 - an explanation of why these data are applicable and satisfactory for the new indications.
- Patent certification or notification

Do not submit:

- Labels. The only change you may make to labels is the pack size descriptor if additional pack sizes are required as a consequence of the extension of indications. See [PIEP: Additional pack sizes resulting from extension of indications to align with a reference product](#).

Associated changes

If you are applying for additional pack sizes as a result of the extension of indications use associated variation type:

- [PIEP: Additional pack sizes resulting from extension of indications to align with a reference product](#)

2.3 Associated changes to product information (PI)

For information about associated changes see:

- [Associated changes](#) in this guidance
- Associated changes in the [Variations to prescription medicines – excluding variations requiring evaluation of clinical or bioequivalence data; Process guidance](#).

2.3.1 Changes associated with PIES

PIEP: Additional pack sizes resulting from extension of indications to align with a reference product

Additional pack sizes as a result of [PIES: Extension of specific indications to align with a reference product](#):

Requires update to ARTG data: Pack Size & Poison Schedule.

Conditions

- Additional pack size(s) are:
 - already registered to the reference medicine
 - necessary for consumer compliance with one of the new indications
 - not associated with any changes to container material, size or shape, or any other change that may require the provision of stability data.
- The only change to the label is the pack size descriptor and the labels comply with the current labelling order.

Data requirements

You must submit:

- Justification of why you are applying for additional pack sizes.

Do not submit:

- Labels. The only change you may make to labels is the pack size descriptor.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Scientific Operations Management Section/SEB	June 2017
V2.0	Inclusion of notifiable variations to registered medicines. Minor amendments to phrasing and layout.	TGA	December 2017
V3.0	Amended title Inclusion of Extension of indications to align with a reference product Additional information on: <ul style="list-style-type: none"> variation types that are associated with a mandatory PAR field update changes that do not need to be notified to the TGA new variation types (including Associated changes and SARO). Minor clarifications and corrections to phrasing and layout.	Scientific Evaluation Branch (SEB)	July 2019
V3.1	Minor clarifications and corrections to: <ul style="list-style-type: none"> API changes that do not require reporting to the TGA CCSC: Container/closure system - changes to container components and/or dimensions. 	Scientific Evaluation Branch (SEB)	January 2020

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