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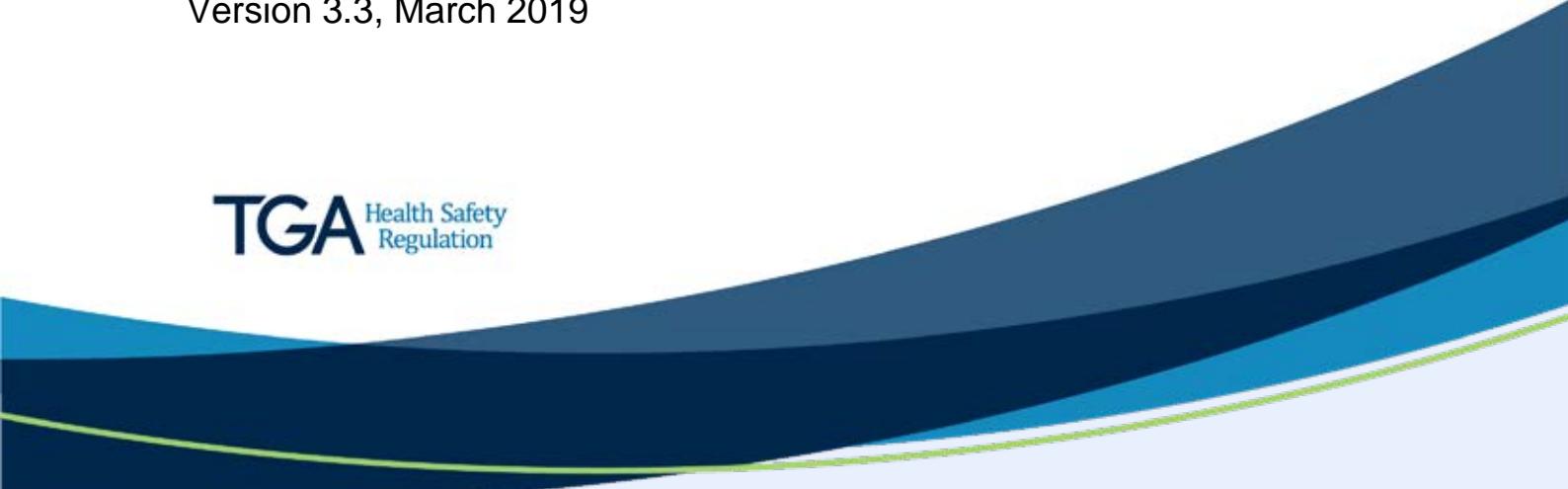
Therapeutic Goods Administration

Risk management plans for medicines and biologicals

Australian requirements and recommendations

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TGA Health Safety
Regulation



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About this guidance

This guidance is for sponsors of prescription medicines and biologicals making applications to enter or vary Australian Register of Therapeutic Goods (ARTG) entries. It describes the risk management plan (RMP) requirements.

This guidance:

- describes what an RMP is
- explains when you must submit an RMP with an application for registration, inclusion or variation in the ARTG
- describes what to include in an RMP and the required format for RMPs
- details special requirements for RMPs for biologicals and generics
- outlines how we evaluate RMPs
- explains when to submit RMP updates after regulatory approval, and
- describes how we monitor your compliance with RMP commitments.



In this guidance, 'RMP' refers to the RMP format requested by the TGA.

This typically comprises both the European Union (EU) RMP and an Australia-specific annex (ASA).

For more information, see [RMP format](#).

The RMP documents the risk management system required to; identify, characterise and minimise a product's important risks.

The TGA (we) require RMPs be submitted for evaluation with certain higher-risk applications to enter a medicine or biological in the ARTG or to vary an ARTG entry (see [When an RMP is required](#)).

Throughout the lifecycle of the product, RMPs must be maintained and important updates submitted to the TGA (us) for evaluation (see [Submitting RMP updates after regulatory approval](#)).

You, as the sponsor, are responsible for the RMP, including:

- developing the RMP
- updating the RMP as new safety information emerges
- implementing the activities and interventions outlined in the RMP
- collecting and analysing information to monitor the effectiveness of these activities and interventions, and
- communicating this information to us in a timely manner

Further information

For further information about risk management plans, see the following TGA guidance:

- [Mandatory requirements for an effective application](#)
- [CTD module 1: Administrative information and prescribing information for Australia](#)
- [Pharmacovigilance responsibilities of medicines sponsors: Australian recommendations and requirements](#)
- [Biovigilance responsibilities of biologicals sponsors: Australian requirements and recommendations](#)
- Template for the [Australia-specific annex](#) to the risk management plan
- [Biosimilar medicines regulation](#)

The following [TGA-adopted EU guidelines](#) are relevant:

- EMA/838713/2011 Guideline on good pharmacovigilance practices (GVP) Module V — Risk management systems
- EMA/204715/2012 Guideline on good pharmacovigilance practices (GVP) Module XVI — Risk minimisation measures: selection of tools and effectiveness indicators
- EMA/488220/2012 Guideline on good pharmacovigilance practices (GVP) Product- or Population-Specific Considerations I: Vaccines for prophylaxis against infectious diseases
- EMEA/359381/2009 CHMP Recommendations for the Pharmacovigilance Plan as part of the Risk Management Plan to be submitted with the Marketing Authorisation Application for a Pandemic Influenza Vaccine

Useful publication:

- [Practical approaches to risk minimisation for medicinal products](#) — Report of CIOMS Working Group IX

The following EU guidelines have not been adopted by the TGA, but are also relevant to RMPs:

- [EMEA/149995/2008](#) Guideline on safety and efficacy follow-up — risk management of advanced therapy medicinal products
- [EMA/PRAC/613102](#) Guidance on the format of the risk management plan (RMP) in the EU — in integrated format
- [EMA/PRAC/222346](#) Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU

What is an RMP?

An RMP is a detailed description of a risk management system. The RMP contains:

- the identification or characterisation of the safety profile of the medicine or biological, with emphasis on;
 - important identified risks
 - important potential risks
 - missing information
 - which safety concerns need to be managed proactively or further studied (the ‘safety specification’)

and

- a set of product vigilance and risk minimisation activities designed to identify, characterise, and manage the important safety concerns relating to the medicine or biological, including the assessment of the effectiveness of these activities and interventions.

These activities may be classified as:

- ‘routine’ (which apply to all products)
- or
- ‘additional’ (see Table 1 for examples).



In this document **‘Product vigilance’** is used to encompass **both** pharmacovigilance (for medicines) and biovigilance (for biologicals)

Table 1: Examples of routine and additional product vigilance and risk minimisation activities

	Routine	Additional
Product vigilance	<ul style="list-style-type: none"> • Collection, follow-up and reporting of adverse events • Continuous monitoring of the benefit-risk profile 	<ul style="list-style-type: none"> • Clinical trials • Post-authorisation safety studies • Patient registries
Risk minimisation	<ul style="list-style-type: none"> • Product Information • Consumer Medicine Information • Pack size • Packaging and labelling • Medicine scheduling 	<ul style="list-style-type: none"> • Educational programs or tools for health professionals and/or consumers • Controlled access programs • Pregnancy prevention programs • Direct healthcare professional communication

The RMP covers the life cycle of the product. You must update the RMP as new knowledge and understanding of the products' safety profile and benefit–risk balance become known.

You should refer to the following EMA guidelines for information about the principles of risk management and the content of risk management plans.

- [EMA/838713/2011](#) Guideline on good pharmacovigilance practices (GVP) Module V — Risk management systems
- [EMA/204715/2012](#) Guideline on good pharmacovigilance practices (GVP) Module XVI — Risk minimisation measures: selection of tools and effectiveness indicators
- [EMA/PRAC/613102](#) Guidance on the format of the risk management plan (RMP) in the EU — in integrated format

An RMP is not a substitute for other product vigilance activities. You **must also** fulfil the pharmacovigilance or biovigilance responsibilities, as described in:

- [Pharmacovigilance responsibilities of medicine sponsors — Australian recommendations and requirements](#)
- [Biovigilance responsibilities of sponsors of biologicals — Australian requirements and recommendations.](#)

Why RMPs are required

A medicine or biological is approved for registration or inclusion in the ARTG if the benefit–risk balance is favourable for the target population in the specified indication(s), at the time of approval.

All products have possible safety concerns, with varying degrees of:

- severity
- likelihood of occurrence
- impact on the individual patient
- impact on public health.

Some adverse reactions and risks are not known at the time of approval (because of the limited duration, size and diversity of the patient population included in clinical trials) and will only be identified and characterised during post-approval use.

An RMP describes how safety concerns will be characterised, monitored and mitigated once the product is supplied. This helps ensure that the benefit–risk balance remains favourable or identifies if the benefits no longer outweigh the risks.

When an RMP is required

An RMP is required with all submissions for:

- registration of new chemical entities
- provisional registration of a new medicine
- a provisional extension of indication

Some application types (for example, extensions of indications and major variations) do not require an RMP in all cases. An RMP may be required for some application types as described in [Table 2 - RMP requirements by application type](#), or with applications if a safety concern is identified for which additional pharmacovigilance or risk minimisation may be required.

We may also request an RMP or updated RMP at any stage of a product's life-cycle, during both the pre-approval and post-approval phases. You will be notified in writing and given our reason(s) for the request.

Refer to [Application types that do not always require an RMP](#) for further information about how to determine whether an RMP is required for your application types, and how to seek advice from the TGA.

Table 2: RMP requirements by application type

Application type	RMP required?
Type A – New chemical entity/biological* medicine (provisional, priority or standard pathway), excluding biosimilars	Always.
Type A, C and F for vaccines	<p>For all new vaccines, extensions of indication and some major variations (see When is an RMP required for a variation?).</p> <p>An updated RMP is required with or before strain change applications for seasonal influenza vaccines if changes to the pharmacovigilance plan are required, as described in the TGA annotations to EMA/PRAC/222346 Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU. The TGA will evaluate the updated RMP independently of the evaluation of the seasonal strain variation.</p>
Biologicals*	<p>For all new class 3 and 4 biologicals and for significant extensions of indication and other major variations as for prescription medicines (see When is an RMP required for a variation?).</p> <p>On request for class 2 biologicals, when the TGA identifies a safety concern for which additional biovigilance or risk minimisation may be required.</p> <p>Not required for class 1 biologicals.</p>

Application type	RMP required?
Type B – New fixed combination of active ingredients	Only in certain circumstances (see When is an RMP required for a new combination of active ingredients?).
Type C – Extension of indication	<p>When the proposed target population differs materially from the previously approved target population (see What is a significant change in indication?) or when the extension of indication has a current provisional determination.</p> <p>A provisional extension of indication will always require an RMP.</p>
Type D – Generic	Only in certain circumstances (see When is an RMP required for a generic?).
Type A – Biosimilar	Required, unless the originator has no additional pharmacovigilance or risk minimisation activities (see When is an RMP required for a biosimilar?).
Type F – Major variation	If the variation leads to new or heightened risks (see When is an RMP required for a variation?).
Category 3 application	An RMP is not required unless we request one. If the variation results in the need to amend additional risk minimisation materials, then these should be submitted for review (see When is an RMP required for a variation?).
Type J – Change to product information requiring evaluation of data	Only if requested by TGA.
Safety-related requests (SRR)	<p>An updated RMP may be required as a result of a safety-related request (for example if there have been related changes to the summary of safety concerns, pharmacovigilance plan or risk minimisation plan). The RMP should be submitted as a post-approval update (see Submitting RMP updates after regulatory approval).</p> <p>It may be provided with the SRR or after approval of the SRR and will be evaluated independently of the SRR.</p>

*Biological medicines (for example, vaccines, plasma derivatives and products of the fermentation of recombinant cell lines) are regulated as prescription medicines and are distinct from biologicals, which are human cell and tissue products.

Application types that do not always require an RMP

For certain application types, we determine the need for an RMP to be submitted on a case-by-case basis. Our primary considerations for the following types of applications are:

- whether the proposed change leads to new safety concerns, heightened risk for patients or new items of missing information
 - extensions of indication
 - new combinations of active ingredients
 - major variations
- whether there are known safety concerns for the originator product for which additional activities are needed, or whether there are differences in their proposed usage that may lead to a new safety concern
 - generics
 - biosimilars

If you are unsure whether an RMP will be required, we recommend that you [contact us](#) for advice as early as possible before you lodge your pre-submission planning form (for medicines) or submit your application (for biologicals) (see [If you're not sure an RMP is required](#)).

What is a significant change in indication?

A significant change in indication occurs when the proposed target population differs materially from the previously approved target population for a product.

This may include (but is not limited to) a:

- new disease area (e.g. seeking approval for a rheumatology indication for a product with an approved oncology indication). Extending the indication within the same disease area would not usually be considered a significant change. For example, two different solid tumour indications, or two related inflammatory conditions would not be considered significantly different if the line of treatment and patient populations are otherwise similar. However, if the extension was associated with another significant change, such as a new dose form or different dosing regimen, then an RMP may be required.
- new age group (e.g. paediatric indication)
- change from treatment of severe disease to treatment of a less severely affected population
- change to a combination treatment regimen (particularly for oncology and antiviral indications, or where there is a significant safety concern with one or more of the included medicines)

When is an RMP required for a new fixed combination of active ingredients?

New [fixed combinations](#) of active ingredients will require an RMP when:

- one of the active ingredients is a new chemical entity
- one or more of the active ingredients requires additional risk minimisation
- the indication of the combination differs from the indications of the individual active ingredients

An RMP may also be required if the combination leads to a new safety concern, or if there are new safety concerns for any of the individual active ingredients.

When is an RMP required for a generic?

An RMP is **not** required for generic medicines, unless:

- there is an RMP for the originator product **and** a safety concern has been identified for which additional risk minimisation activities are being conducted, or
- there is no RMP for the originator product, but there are safety concerns with the substance that have required specific risk minimisation activities. This includes, but is not limited to, thalidomide, leflunomide, clozapine, lenalidomide and isotretinoin and derivatives of these products, or
- if the introduction of the generic may lead to a new safety concern, such as medication error (for example, different preparation instructions) or off-label use (for example, restricted indications), or
- we request one

For information about what to include in RMPs for generics, see [Requirements for RMPs for generics](#).

When is an RMP required for a biosimilar?

An RMP may be required if the biosimilar does not have all of the same indications and presentations as the originator product, so the need for risk minimisation for safety concerns resulting from medication error can be considered.

An RMP is **not** required for a biosimilar when:

- there is an RMP for the originator product and there are neither additional pharmacovigilance activities nor additional risk minimisation activities being conducted, **and**
- the biosimilar will have the same indications (without omission of any indications), dosage forms, strengths and routes of administration as the originator product

If there is no RMP for the originator product then an RMP for a biosimilar version would generally not be required unless there is a significant difference in the use of the medicine.

If you are unsure about the RMP requirement for your biosimilar product then [contact us](#) prior to preparing your application.

When is an RMP required for a variation?

You should submit an RMP with an application for a **major** variation if the variation results in a new or heightened risk.

For example:

- a new dosage form or route of administration with inherently higher risk (for example, injection vs tablets)
- a new higher strength leading to a higher risk of medication error that could have a significant effect on patients
- a larger pack size if this may increase risk

For **minor** variations, an RMP is not required unless we request one, but you should consider whether the changes result in a need to amend risk minimisation materials.

For example:

- category 3 applications for changes to container type or pack size may lead to a need to change patient guides or instructions for use. You should include in your submission any risk minimisation materials with proposed amendments resulting from the variation. You do not need to submit an updated version of the RMP for evaluation for a category 3 application unless we ask for one.

If an RMP is not required

You must still comply with routine product vigilance and risk minimisation requirements if an RMP is not required. Routine product vigilance (called pharmacovigilance for medicines and biovigilance for biologicals) requirements are set out in:

- [Pharmacovigilance responsibilities of medicines sponsors: Australian recommendations and requirements](#)
- [Biovigilance responsibilities of sponsors of biologicals – Australian requirements and recommendations](#)

Requirements include, but are not limited to:

- [telling us](#) who your Australian pharmacovigilance or biovigilance contact person is through the TGA Business Services electronic portal
- [submitting](#) any serious adverse reaction reports to us
- [notifying us](#) of any significant safety issues you identify
- [keeping records](#) pertaining to the reporting requirements and safety for your medicine (under Subsection 28(5)(ca) of the *Therapeutic Goods Act 1989* (the Act))
- answering any request from us for additional information fully and within the specified timeframe (under Subsection 31(1) of the Act)

If you are not sure an RMP is required

If you are not sure whether you should submit an RMP with an application, [email the RMP coordinator](#) describing the proposed application before you complete the Pre-submission Planning Form (for medicines) or submit your application (for biologicals).

We will assess the requirement for an RMP, taking into account the information you provide, and notify you in writing. If no RMP is required, you can include our advice in Module 1.8.2 of your submission, as described in [CTD Module 1: Administrative information and prescribing information for Australia](#).

Even if submission of an RMP is not required, we expect that you will continue to maintain any existing RMP relating to the product(s) (see [Submitting RMP updates after regulatory approval](#)).

How to tell us if you will be submitting an RMP with an application

Medicines RMP submission

Ensure you accurately indicate whether you will be submitting an RMP by completing the information relating to CTD Module 1.8 in the [Pre-submission Planning Form \(PPF\)](#).

Provide a justification if you think an RMP is not necessary. If we advised you that an RMP would not be required before you submitted the PPF, please state this in the PPF.

We recommend that you contact us for advice before submitting the PPF if you are unsure if an RMP will be required.

Assessing the requirement for an RMP

We will consider the information you provide in the PPF and tell you whether you need to submit an RMP in the planning letter (standard applications) or notification letter (PPF only applications).

If we conclude that you should submit an RMP with the application, but you have indicated in the PPF that you do not intend to submit an RMP, we will tell you that an RMP must be submitted for evaluation. If we previously advised that an RMP was not required, then we will work with you to develop an agreed timeframe for submission.

If you indicate you will be submitting an RMP, but we conclude that it is not a requirement, we will tell you that you do not need to submit an RMP.

If you submit an RMP with a 'PPF only' application, and we determine that it is not a requirement, we will tell you that your RMP will not be evaluated for the purposes of the application. If your product is already registered, we will ask you to consider whether you should submit your current RMP as a post-approval update. If so, you should complete and submit the [Submission of an updated RMP](#) form (see [Submitting RMP updates after regulatory approval](#)).

For products approved with an RMP as a condition of registration, the RMP should be maintained throughout the remainder of that product's lifecycle (even if we do not request an RMP for evaluation with applications for extensions of indication or other changes).

Biologics RMP submission

We will assess the requirement for an RMP during any pre-submission process or during the screening of an application following receipt.

RMP format

You should submit the most up-to-date version of the EU RMP relevant to the submission, accompanied by an Australia-specific annex (ASA) to document the differences between the plan for Australia and the EU RMP. An EU RMP that is under consideration by the EMA is acceptable if there is no approved version of the EU RMP.

If no EU RMP exists, then you may submit an alternative RMP, such as a global or core RMP. However, it must:

- cover all of the modules of the EU RMP,
- be presented in the current EU RMP format, and
- be accompanied by an ASA

The format for the EU RMP is described in the following guidance:

- [EMA/838713/2011](#) Guideline on good pharmacovigilance practices: Module V - Risk management systems, and
- [Guidance on format of the risk management plan \(RMP\) in the EU](#) — in integrated format. It is acceptable to submit RMPs in the format consistent with either the first revision of the template (EMA/465932/2013 Rev 1) or the second revision of the template (EMA/PRAC/613102/2015 Rev 2).

It is acceptable to submit an 'Australia-specific RMP' if no EU, core or global RMP exists. This is the only situation in which an ASA is not required.

Risk management plans for biologicals should include additional sections about possible risks specific to a biological. Refer to [Requirements for RMPs for biologicals](#) for further information.

Risk management plans for generics should follow either the integrated format or abridged format for generics. Refer to [Requirements for RMPs for generics](#) for further information.

You should contact us for advice if you are uncertain about which RMP you should submit.

Requirements for RMPs for biologicals

In an RMP for a biological (human cell or tissue product), include discussion of possible risks specific to biologicals that may not apply to other therapeutic products. Refer to:

- [EMA/838713/2011](#) Guideline on good pharmacovigilance practices (GVP) Module V — Risk management systems
- [EMEA/149995/2008](#) Guideline on safety and efficacy follow-up - risk management of advanced therapy medicinal products, which contains guidance about:
 - the possible risks specific to biologicals
 - biovigilance, efficacy follow-up and risk minimisation activities of particular relevance to biologicals

The concepts and information in these EMA guidelines are applicable to biologicals, despite being focused on medicines and advanced therapy medicinal products (ATMPs), which include a narrower group of products than those regulated under the [Australian biologicals framework](#).

The following information is required for RMPs for biologicals. These additions may be included in the EU RMP or included as an attachment to the Australia-specific annex.

If an RMP section is not applicable to a particular product, do not omit the section, but instead state this in the RMP and provide a justification.

1. consider the specific risks of biologicals. This can be in the safety specification in the EU RMP or in a separate attachment to the Australia-specific annex. For guidance on risks to address refer to:
 - [EMEA/149995/2008](#) Guideline on safety and efficacy follow-up - risk management of advanced therapy medicinal products, Section 8.1 Safety specifications
2. include a section 'Evaluation of the need for efficacy follow-up' in either RMP Part II or attached to the Australia-specific annex. When a need for efficacy follow-up is identified, the efficacy follow-up plan should be included as an attachment to the Australia-specific annex. Refer to:
 - [EMEA/149995/2008](#) Guideline on safety and efficacy follow-up – risk management of advanced therapy medicinal products, Section 8.4 Evaluation of the need for efficacy follow-up
3. provide a detailed description of the sponsor's biovigilance system in Australia either in the Australia-specific annex (where an EU, global or core RMP is provided) or in RMP Part III Pharmacovigilance plan (when an Australian RMP is provided). Refer to:
 - [Biovigilance responsibilities of sponsors of biologicals: Australian requirements and recommendations](#)

The description of the biovigilance system should include:

- a summary of the sponsor's routine biovigilance activities
- details of the elements of the biovigilance system needed to support the additional biovigilance activities included in the RMP
- details of procedures for traceability of products from donor to recipient, and recipient to donor, to investigate and act on possible disease transmission

4. in the biovigilance plan described in RMP Part III or in the Australia-specific annex, include consideration of safety follow-up issues relevant to biologicals. Refer to:
 - [EMEA/149995/2008](#) Guideline on safety and efficacy follow-up – risk management of advanced therapy medicinal products, Section 8.3 Pharmacovigilance plan (incorporating safety follow-up)
5. when developing the risk minimisation plan, consider the guidance provided on reducing particular risks of a biological product. Refer to:
 - [EMEA/149995/2008](#) Guideline on safety and efficacy follow-up – risk management of advanced therapy medicinal products, Section 8.5 Risk Minimisation plan

Requirements for RMPs for generics

RMPs for generics should be submitted in the integrated format (see [Guidance on the format of the risk management plan in the EU — in integrated format \(Rev 2\)](#)).

You should submit the most recent EU RMP, with an ASA, unless there is no EU RMP available, in which case you should submit a core or global RMP with an ASA, or an Australia-specific RMP if no core or global RMP is available.

There is specific guidance regarding the content of the Australia-specific annex for generics. See the [Template](#) for the Australia-specific annex to the risk management plan for details.

You should refer to the guidance in [Guideline on good pharmacovigilance practices \(GVP\) Module V](#), section V.C.1.1.1 about parts of the RMP to be included for generics.

Safety specification

Align the summary of safety concerns for the generic with that of the originator, by referring to sources such as:

- the [Australian Public Assessment Report \(AusPAR\)](#)
- the European Public Assessment Report (EPAR)
- the [list of safety concerns per approved RMP of active substances per product](#), published by the Co-ordination Group for Mutual recognition and Decentralised Procedures — Human

Consider whether there are any safety concerns associated with the generic product, for example:

- if introduction of a generic in a different administration device could increase the risk of medication error with a significant impact on public health or for the individual (for example, lack of efficacy for a life-threatening condition or an increased risk of adverse effects)
- if introduction of a generic without presentations suitable for use by particular patient populations, such as children or people with particular conditions, may require additional education of health professionals

Pharmacovigilance plan

If there are specific adverse-event follow-up forms implemented for the originator, these should also be implemented for the generic.

Risk minimisation plan

An RMP will generally only be required for a generic:

- when the originator has been required to undertake additional risk minimisation activities, or
- where there may be a need for additional risk minimisation activities to address a safety concern specific to the generic

Therefore, in the risk minimisation plan in the RMP/ASA you should:

- describe the proposed additional risk minimisation activities for the generic

- where known, state whether these differ from the additional risk minimisation activities implemented for the originator, and if so
 - provide a justification for each difference

We evaluate the need for additional risk minimisation activities to be undertaken for generic medicines on a case-by-case basis, taking into account factors such as:

- the nature and purpose of the additional risk minimisation activities required for the originator
- whether the additional risk minimisation activities required for the originator are ongoing
- whether the relevant safety concerns are adequately mitigated by routine clinical practice
- any safety concerns specific to the generic

Additional risk minimisation materials for generics should cover the same key safety messages as those for the originator, and any safety concerns specific to the generic. The key safety messages should be included in the Australia-specific annex.

As the risk minimisation in place in Europe is generally similar to that in Australia, risk minimisation materials implemented in the United Kingdom on the [electronic Medicines Compendium website \(eMC\)](#) website can be a useful source of information relating to the additional risk minimisation activities in place for the originator.

Australia-specific annex to the EU RMP

The Australia-specific annex (ASA) provides details not included in the EU RMP that enables the EU RMP (or, core or global RMP if no current EU RMP exists) to be adapted to the Australian context.

The ASA is required:

- to document any differences in safety concerns between the EU and Australia (which may include differences in the frequency, severity or nature of safety concerns resulting from differences in the epidemiology of the indication and target population) and ensure that these are taken into account in determining an adequate risk management system
- to document any risk management activities not reflected in the EU RMP that are required to adequately address the safety concerns in Australia (such as differences between the EU SmPC and Australian PI in the wording of precautions or contraindications, or additional pharmacovigilance activities required by the TGA)
- to record details of the dissemination and evaluation of effectiveness of risk minimisation activities in Australia (which would be determined at a national level in the EU and are not reflected in the EU RMP)
- to record milestones and timelines for reporting on additional pharmacovigilance and risk minimisation activities to the TGA

Information needed in the ASA

The ASA should provide Australian-specific information that is important in assessing:

- the risk in Australia (and therefore appropriateness of proposed plans and activities)
- whether there are any safety concerns that may be unique to Australia
- the relevance of international product vigilance and risk minimisation activities to Australia, and reasons for any differences from activities planned overseas

When is an ASA required?

You must submit an ASA with the EU RMP (or alternative RMP where no current EU RMP exists).

Are there any exceptions to this requirement?

The only situation where an ASA is not routinely required is if the RMP has been prepared specifically for Australia (because there is no EU RMP, core RMP or global RMP).

Format and content of the ASA

You should prepare the ASA using the [template](#) (which includes guidance for drafting the ASA). If you choose not to use the template provided, then you must ensure all the information required in the template, is included in your ASA.



The latest version of the template was published in March 2019.

New ASAs submitted with applications after 31 March 2020 should contain the information required in the updated version of the template.

ASAs first submitted prior to 31 March 2020 may be maintained in the format described in v3.1 (November 2017) of *Risk management plans for medicines and biologicals: Australian requirements and recommendations*.

You should include, as appendices to the ASA:

- additional risk minimisation materials to be implemented in Australia,
- targeted follow-up forms to be used in Australia, if they are not attached to the EU RMP, and
- protocols for any additional pharmacovigilance activities that appear only in the ASA.

Evaluation process for Risk Management Plans

RMPs are evaluated during the prescription medicines registration and biological inclusion processes.

Who is responsible for evaluating the RMP?

The Risk Management Plan Evaluation Section is primarily responsible for evaluating the RMP. The clinical and non-clinical evaluators provide advice to the RMP evaluator about the adequacy of the summary of safety concerns in the RMP.

What is considered in the evaluation?

In evaluating the RMP, we will consider:

- the adequacy of the summary of safety concerns at the time of application
- identification of additional safety concerns during the course of our evaluation of other modules included in the application (which may result in recommendations to amend the summary of safety concerns originally submitted)
- the adequacy and appropriateness of the proposed product vigilance and risk minimisation activities for the specified safety concerns

RMP evaluation process for medicines and biologicals

Table 3 below describes the RMP evaluation process for prescription medicines and biologicals. For medicines, the process reflects the standard application pathway. Refer to other TGA guidance for information about RMP evaluation during the [priority](#) or [provisional](#) or [comparable overseas regulator](#) pathways.

Table 3: RMP evaluation process steps for prescription medicines and biologicals

Step	Prescription medicine process	Biologics process
Round 1 evaluation	<p>Recommendations for amendments:</p> <ul style="list-style-type: none"> Summary of safety concerns Consumer Medicine Information Product Information Risk minimisation plan Pharmacovigilance plan <p>If available, advice from the clinical and nonclinical evaluations will be incorporated at this stage.</p> <p>The report is provided at Milestone 3.</p>	<p>Recommendations for amendments:</p> <ul style="list-style-type: none"> Summary of safety concerns Patient information leaflet Product Information Risk minimisation plan Biovigilance plan

Step	Prescription medicine process	Biologics process
Round 1 report	Response to request for information (s31)	Response to request for information (s32JA)
Round 2 evaluation	<p>Reconciliation of s31 response to issues raised in round 1 report.</p> <p>Incorporation of further advice from:</p> <ul style="list-style-type: none"> • clinical evaluator • non-clinical evaluator <p>Questions for expert advisory committee determined, if advice required</p> <p>Note: the report is usually issued two weeks after Milestone 5 to allow for incorporation of final clinical and non-clinical advice.</p>	<p>Reconciliation of s32JA response to issues raised in round 1 report.</p> <p>Incorporation of advice from:</p> <ul style="list-style-type: none"> • clinical evaluator • non-clinical evaluator <p>Questions for expert advisory committee determined, if advice required</p>
Post-Round 2 evaluation	Consider pre-ACM/ACV response	Consider pre-ACB response
Expert advisory review (if required)	<p>Advisory Committee on Medicines (ACM) or Advisory Committee on Vaccines (ACV)</p> <p>If required, committee advice will normally be sought at Milestone 6</p>	Advisory Committee on Biologicals (ACB)
Final reconciliation	Final RMP negotiation, considering any ACM/ACV advice, the post-ACM/ACV response and final PI and CMI modifications	Final RMP negotiation, considering any ACB advice, the post-ACB response and final PI and CMI modifications
Decision to approve	Implementation of the RMP is imposed as a condition of registration at the decision date (Milestone 7)	Implementation of the RMP is imposed as a condition of inclusion
Post-approval	<p>Ongoing pharmacovigilance and risk-minimisation:</p> <ul style="list-style-type: none"> • Periodic Safety Update Report (PSUR) submission for a specified period of time • RMP updates submitted as per guidelines for the life cycle of the product 	<p>Ongoing biovigilance and risk-minimisation:</p> <ul style="list-style-type: none"> • Periodic Safety Update Report (PSUR) submission for a specified period of time RMP updates submitted as per guidelines for the life cycle of the product

The roles of the Advisory Committees

In some cases, we will seek advice from one (or more) of our advisory committees on the adequacy and appropriateness of the safety specifications, and product vigilance and risk minimisation activities, detailed in the RMP.

- [Advisory Committee on Medicines \(ACM\)](#)
- [Advisory Committee on Vaccines \(ACV\)](#)
- [Advisory Committee on Biologicals \(ACB\)](#)

We notify the sponsor in the RMP report when a product is to be referred to one or more of these committees.

If advice is required

We will provide the questions to the sponsor prior to the committee meeting. However, in accordance with the prescription medicines registration process and the biologicals inclusion process, there is no opportunity to submit additional or supplementary data at this stage prior to committee review.

Medicines

We would usually seek expert advice on the risk management plan at the committee advice phase ([Milestone 6](#) of the prescription medicines registration process). In some cases we may seek advice between [Milestone 3](#) and [Milestone 4](#) of the prescription medicines registration process.

Biologics

In some cases we may seek advice between the first and second rounds of RMP evaluation for biologicals.

When does the TGA provide feedback on the evaluation of an RMP?

Medicines

We will issue a full RMP evaluation report, and any recommendations and questions on the RMP, via the single round s31 information requests at Milestone 3, except for applications assessed under the [priority pathway](#), for which the RMP evaluation report will be issued at the conclusion of the evaluation phase.

The relevant recommendations from the clinical and non-clinical evaluation reports, and the sponsor's response to the RMP evaluation report, will be incorporated into the RMP evaluation when available. This may be after Milestone 5 for medicines.

This advice will be provided to the Delegate and sent to the sponsor.

The RMP may be subject to review or consideration by TGA's advisory committees and, in this case, the relevant minutes from the ACM or ACV meeting(s) will be provided to the sponsor.

If there are outstanding issues after the round 2 RMP evaluation, we will conduct further rounds of RMP evaluation as needed. After each round of evaluation, we will send the updated RMP evaluation report to the sponsor. We may also contact the sponsor directly to discuss the outstanding issues.

Biologicals

We will issue a full RMP evaluation report, and any recommendations and questions on the RMP, via the s32JA information request after the first round of RMP evaluation.

The relevant recommendations from the clinical and non-clinical evaluation reports, and the sponsor's response to the RMP evaluation report, will be incorporated into the RMP evaluation when available. This may be after the second round of RMP evaluation.

This final report will be provided to the Delegate, and then sent to the sponsor before any regulatory decision.

The RMP may be subject to review or consideration by the TGA's advisory committees and, in this case, the relevant minutes from the ACB meeting(s) will be provided to the sponsor.

If there are outstanding issues after the round 2 RMP evaluation, we will conduct further rounds of RMP evaluation. After each round of evaluation, we will send the updated RMP evaluation report to the sponsor.

RMP updates during the evaluation process

An updated EU RMP may become available during the evaluation process, either due to sponsor-initiated changes, or changes required as part of the evaluation process in the EU. If you anticipate that this will occur, please advise us in your submission (for example, by including the due date for the updated RMP in your ASA, or including a note to the reviewer).

We may ask you to submit an updated RMP to reflect required changes identified during the evaluation.

Any updated RMP submission requires a:

- summary table of changes between the updated RMP and the last RMP submitted to the TGA
- cover letter stating the reason for submission

It is acceptable to submit an updated version of the RMP with tracked changes or annotated changes, in addition to a clean version.

Maintaining records

Maintain records, in Section 1.1 of the revised ASA template, of:

- when RMPs were submitted to us, and
- the significant changes between each version of the RMP.

Other requirements

- Ensure you reflect any updates to the Product Information (PI), Consumer Medicine Information (CMI) or Patient Information Leaflet that result from the evaluation process in the subsequent version of the ASA. If available, this may be provided with the closing sequence that contains the approved PI and CMI, or at a later date as post-approval RMP update.
- For changes that have no impact on the EU RMP, but affect the ASA, providing an updated ASA is sufficient, with a reference to the current EU RMP version (for example: changes to Australian PI/CMI documents).

- On completion of the evaluation process, you should ensure that a final version of the RMP confirming the agreed pharmacovigilance and risk minimisation activities has been submitted. This may require submission of a revised version that addresses any recommendations made in the round 2 or subsequent evaluation reports.
- We may ask you to provide hard copies of final additional risk minimisation materials and passwords to access electronic materials, when available, for our records.

The RMP in the Australian Public Assessment Report (AusPAR)

The AusPAR will contain a section on pharmacovigilance findings, which will include the summary of the RMP evaluation, including the following key elements:

- the agreed summary of safety concerns
- a summary of the associated pharmacovigilance and risk minimisation activities, including whether additional activities are being conducted to address particular safety concerns

The AusPAR may include:

- timelines for planned activities, such as:
 - reporting dates for key ongoing or planned studies
 - communication program milestones
- any differences between the risk minimisation activities undertaken in Australia compared to the EU

It may also include the key safety messages and outcomes of additional risk minimisation activities.

How is the RMP referred to in the conditions of registration or inclusion?

The latest versions of the RMP and ASA that have been evaluated by the TGA will be included in the conditions of registration or inclusion (taking into account any updates provided during the evaluation process). In some circumstances we may apply a version of the RMP and ASA evaluated as part of a concurrent submission as a condition of registration.

In addition, your written agreements to the RMP evaluator's recommendations during the s31 process or s32JA process (which are not explicitly stated in the RMP document), as well as any further requirements determined by the Delegate, may be included in the conditions of registration or inclusion.

Submitting RMP updates after regulatory approval



The updated RMP is not a replacement for normal mechanisms for informing us about safety-related issues.

Whenever you submit an updated RMP, ensure you:

- use the [form](#) provided to describe why you are submitting the RMP, and provide the form in Module 1.0.1. **and**
- clearly indicate all changes from previous RMPs in the documents (preferably in a summary table, which may be in Annex 8 of the EU-RMP and section 1.2 of the ASA)

When to submit an updated RMP

You must submit an updated RMP and/or ASA when we request it and whenever there is significant change, such as:

- when the summary of safety concerns changes, including when the EMA has approved removal or reclassification of safety concerns
- when an additional product vigilance or risk minimisation activity is ceased, added, or substantially altered for example,
 - if the objectives, patient population or expected completion date of an additional pharmacovigilance activity change or if the pharmacovigilance activity is ceased early
 - if a new additional pharmacovigilance activity is added
 - if you propose to cease an additional risk minimisation activity, add or remove a safety concern from risk minimisation activities, or implement a new additional risk minimisation activity
- for provisionally registered products, if there are any changes to the objectives, population or due date of final results for any of the studies listed in the clinical study plan

You do not need to submit an updated RMP on expected completion of a pharmacovigilance activity that appears in the EU RMP if there are no changes to the summary of safety concerns or risk minimisation plan as a result. You should, however, submit an updated ASA +/- RMP on completion of any additional pharmacovigilance activities that have been implemented at the request of the TGA (which are likely to appear only in the ASA).

We may require an updated RMP to incorporate changes that have already been agreed such as through the evaluation process for registration of a new product, extension of indication or variation, or safety-related request.

Submitting an updated RMP is not a substitute for other regulatory requirements, such as submitting minor variations or safety-related requests, or notifying the TGA of significant safety issues.

You should update your risk management plan when new information becomes available regardless of whether your product is marketed. You should ensure that you always keep your RMP and ASA up to date for your own records and because we may request an updated RMP from you at any time.

Timeframes for submitting updated RMPs

You should seek agreement from the TGA before prematurely ceasing or significantly altering:

- additional risk minimisation that is being undertaken in Australia
- additional pharmacovigilance that is being undertaken in Australia at the request of the TGA

If you are proposing changes to the risk management system in response to a significant safety issue, you should advise the TGA of the significant safety issue within 72 hours, as per the [Pharmacovigilance responsibilities of medicine sponsors](#). You can submit the updated RMP after the response to the safety issue has been agreed with the TGA.

For changes that have been accepted by the EMA and do not affect additional risk minimisation activities being undertaken in Australia or additional pharmacovigilance activities being undertaken in Australia at the request of the TGA, then we recommend that the updated RMP/ASA is submitted within 3 months of the change being accepted by the EMA. If updates to the RMP coincide with an extension of indication or variation for which submission of an RMP is a requirement, then it is acceptable to submit the updated RMP only in support of the application.

What to include with an updated RMP

Please include:

- the completed '[submission of an updated RMP](#)' form in module 1.0.1 describing the reasons for submitting the RMP update,
- an updated ASA with any updated EU RMP submitted, or a statement on the 'submission of an updated RMP' form that the changes to the EU RMP do not warrant any changes to the ASA, and
- a summary of all changes since the previous version (in the EU RMP and/or the ASA).

If only the ASA has been updated, then it is not necessary to resubmit the EU RMP if you have previously provided the EU RMP to the TGA. Ensure you maintain records of when RMPs were submitted to the TGA and the significant changes between each version of the RMP.

How to submit an updated RMP

Each updated RMP and ASA that you submit to the TGA should be submitted as an eCTD/NeeS sequence. The RMP and/or ASA should be in module 1.8.2. An updated RMP not submitted as part of another regulatory activity should be submitted as a standalone sequence with sequence type 'risk management plan'.

If the date for the submission of a Periodic Safety Update Report (PSUR) and the need to update an RMP coincide, both can be submitted at the same time.

If you wish to seek advice from the TGA on the acceptability of proposed changes to the EU RMP and/or ASA before submitting as a sequence, please email your request for advice to the [RMP coordinator](#), describing the proposed changes using the 'Submission of an updated RMP' form, and providing relevant details of and a justification for the changes. If possible, include the draft updated EU RMP/ASA.

An RMP update does not require a minor variation request or notification.

Evaluation of the updated RMP

We will acknowledge receipt of the updated RMP and evaluate the changes. We will contact you to advise acceptance of the changes or request further information. We will not usually give you an evaluation report.

Submitting risk minimisation materials for review

If you are submitting draft risk minimisation materials for review after regulatory approval and there are no changes to the RMP and/or ASA then you do not need to submit an updated RMP and Submission of an updated RMP form. In these cases you should send the materials to the RMP coordinator (RMP.coordinator@health.gov.au) with a covering email providing background to the request for review and your anticipated timeframe for finalising and disseminating the materials.

If we have not previously reviewed drafts of your materials then we recommend that you allow 6 weeks for review and approval to allow for the possibility of multiple rounds of revisions.

If you require rapid review of materials, please contact the RMP coordinator as early as possible prior to submitting the materials so that we can determine a suitable timeframe for submission and assessment.

Periodic Safety Update Reports

A Periodic Safety Update Report (PSUR) is a systematic review of the global safety data of an approved medicine that becomes available to you during a defined time period. PSURs are also referred to as Periodic Benefit–Risk Evaluation Reports (PBRERs).



We will apply the requirement to submit PSURs as a condition of registration.

We will recommend a condition of registration requiring PSURs in the round 2 RMP evaluation report. You should raise any practical issues in relation to the provision of PSURs to avoid the need for varying the condition after registration.

PSURs are required for certain registered medicines. The requirement to submit PSURs can be applied as a condition of registration under section 28(2B) of the Act when the medicine is included on the ARTG.

The TGA has adopted the EU PSUR guidelines with annotations:

- [EMA/816292](#) Guideline on good pharmacovigilance practices (GVP) Module VII - Periodic safety update report

You should also refer to [Pharmacovigilance responsibilities of medicine sponsors](#) for information about content to include in PSURs.

Where we have identified additional safety concerns and these have been included in the ASA, ensure you report these in an attachment to the PSUR.

When PSURs are required

We take a risk-based approach to determining if PSURs should be submitted to the TGA, and the frequency and duration of submission. Factors we consider when determining the appropriate PSUR condition of registration include:

- the availability of safety information about the product
- the nature of the safety concerns associated with the product and their impact on public health
- the potential implications of any changes to the product for the safety profile of the product or availability of information about the safety profile
- whether populations described in missing information (such as children and pregnant women) are likely to use the product after registration
- whether there are safety concerns specific to Australia

We will usually require sponsors to submit PSURs at least annually until the submitted PSURs cover a period of not less than 3 years from the date of approval for:

- new chemical and biological entities,
- extensions of indication and
- major variations,

assessed under the standard or priority registration pathways. After the end of the initial 3-year period we may request submission of additional PSURs if we determine that close monitoring of a product's safety should continue.

For lower-risk extensions of indication and major variations we may request that PSURs be prepared but submitted only when we request them.

For provisionally registered medicines, we will usually require sponsors to submit PSURs regularly for a longer period than the standard 3 years, to account for the provisional registration period, which may last up to 6 years. We may require PSURs for provisionally registered products to be submitted more frequently, for example 6-monthly.

Determining the PSUR condition of registration

For applications for which we evaluate an RMP, we will include a recommendation to the Delegate for a condition of registration requiring PSURs in the round 2 RMP evaluation report. You should raise any practical issues in relation to the provision of PSURs (such as the availability of complete PSURs in the required timeframes) in your response to the round 2 RMP evaluation report to avoid the need for varying the condition after registration.

For products that are approved in the European Union, we will align the reporting requirements and timeframes with those required by the EMA where possible and appropriate.

A PSUR submission does not require a minor variation request or notification.

How to submit a PSUR

You should submit your PSUR as an eCTD/NeeS sequence, as a standalone sequence with sequence type 'periodic safety update report'.

Monitoring compliance with RMP commitments

You are responsible for:

- maintaining the currency of your RMP,
- implementing the risk management activities included in it,
- collecting and analysing information generated by risk management activities to inform adjustment of your risk management system, and
- notifying the TGA of important changes to your RMP

We will undertake periodic desktop audits of documents you have submitted to us to ensure that you are undertaking or have completed risk management activities in accordance with your RMP. In addition, if you are selected for a [pharmacovigilance inspection](#) you may be required to provide evidence to demonstrate your compliance with RMP commitments.

We may contact you if reporting dates for risk management activities are due and we have not received information from you. For example, we may check that:

- additional risk minimisation interventions have been implemented and their effectiveness has been assessed, and any required evaluation reports submitted to us
- you have submitted the study reports of additional pharmacovigilance activities for which submission is required (as described in your ASA or conditions of registration)

You should ensure that your RMP clearly describes the timeframes for completing risk management and pharmacovigilance activities, and how and when the outcomes will be reported to the TGA. You may need to submit an updated RMP to us at the completion of the evaluation process to reflect any changes required during the round 2 evaluation.

If you are unable to meet a commitment described in your RMP, you should notify us as soon as possible, and provide us with a proposal for amendments to your RMP, with a justification (see [Submitting RMP updates after regulatory approval](#)).

Compliance and enforcement

The Regulatory Compliance Framework sets out the TGA's overall approach to compliance.

If we identify that you have not undertaken your risk management commitments in accordance with your RMP we will generally, in the first instance, work with you to address the deficiencies.

If we identify significant non-compliance with your risk management commitments we can:

- cancel or suspend medicines from the ARTG for refusing or failing to comply with a condition of registration or listing, under subsections 29D(1)(b) and 30(2)(c) of the Act
- prosecute offences related to not complying with conditions of registration or listing, under Section 21A of the Act

We publish information about regulatory compliance decisions and actions, such as compliance undertakings, cancellations and suspensions, on our website.

Risk Management Plan – Australia-Specific Annex

Product details

Active ingredient(s) (INN):	
Product name(s):	
Sponsor name:	
ASA version number:	
ASA version date:	
Related EU-RMP version*:	Version #.# (date, data lock point)
Pharmaco-therapeutic group (ATC Code):	

*Can be changed to 'core' or 'global' RMP if no EU-RMP is available

1. Product overview

1.1. History of RMPs submitted in Australia

In this section, provide a tabulated history of EU RMP and ASA versions previously submitted for evaluation in Australia, with a summary of changes between versions, unless this is clearly indicated in the EU RMP. An example table format is shown below.

State whether the medicine is currently, or is expected to be, included in the Black Triangle Scheme in Australia.

Table 1: History of RMPs submitted in Australia (example)

EU-RMP version	ASA version	Date Submitted	Application or update	Major changes to the ASA/EU-RMP* from previous version
EU-RMP 0.5	ASA v1.0	5/2/16	PM-2016-#####-1-1	<i>Draft EU RMP, first ASA version</i>
EU-RMP 1.0	ASA v1.0	10/6/16	PM-2016-#####-1-1	<i>First approved EU RMP submitted with s31 response</i>
EU-RMP 1.5	ASA 1.1	5/6/17	RMP update	<i>Changed 'Hepatotoxicity' from important potential risk to important identified risk in line with EU RMP under evaluation</i>
EU-RMP 2.0	ASA 1.5	14/9/18	PM-2018-#####-1-1	<i>Extension of indication to psoriatic arthritis. No change in safety concerns or additional risk minimisation activities.</i>

*it is acceptable to refer to the table in Annex 8 of the EU RMP if changes to the EU RMP are clearly indicated there.

2. Safety specification

2.1. Epidemiology of the indication(s) and target population(s)

Provide a brief summary of Australian epidemiological information, where available, for each indication, commenting on whether there are any important differences between Australia and the EU in:

- incidence and prevalence
- demographics of the target population (age, sex, race/ethnic origin)
- risk factors for the disease
- mortality and morbidity (natural history)
- main treatment options

This section should include information on the use of the product in Australia, relevant to assessing the adequacy of the risk management system in Australia, such as:

- the proposed setting of use of the product (hospital, home, specialist treatment centre, etc) and the types of health professionals who will prescribe and be involved in the product's use
- whether use in rural or remote settings presents any challenges to management of risks (such as monitoring and follow-up)
- whether use of the product relies on or is affected by access to diagnostic tests or other technologies that may not be widely available
- whether there are specific risk management considerations for Aboriginal or Torres Strait Islander people (such as a higher prevalence of risk factors for important identified or important potential risks) or other groups
- whether there are any differences in Australia that may affect the likelihood of medication errors or misuse for illegal purposes

For generic or biosimilar medicines, or fixed-dose combination products not including a new chemical entity, a summary of epidemiology is not required in the Australia-specific annex. However, this section should identify and discuss any differences in indications and presentations of the generic or biosimilar to the innovator and other generic or biosimilar versions of the medicine. If there are differences, the impacts of these differences should be considered, for example:

- potential harms from foreseeable off-label use (for example in a patient group for which the innovator provides a specific presentation, but this presentation is not planned for the generic or biosimilar version of the medicine)
- potential for medication error

2.2. Summary of the safety concerns

State clearly and justify any differences between the summary of the safety concerns in the EU RMP and the summary of safety concerns proposed for Australia.

If you propose to omit any of the risks that appear in the EU RMP from the Australian summary of safety concerns, or to classify any of the risks differently, provide a justification.

If there are any Australia-specific safety concerns, provide further information in section 2.2.1.

2.2.1. Australia-specific safety concerns

Include details of any safety concerns for Australia that are additional to those proposed in the EU-RMP. This should include:

- why the additional safety concern is included in the ASA (e.g. TGA requirement, concern is specific to the Australian population)
- a detailed description of the safety concern

The Australia-specific safety concern(s) should be described in the same detail as used in the EU-RMP, as shown below:

<Australian important identified/potential risk>

Potential mechanisms

Evidence source(s) and strength of evidence

Characterisation of the risk

Risk factors and risk groups

Preventability

Impact on the risk-benefit balance of the product

Public health impact

<Australian missing information>

Evidence source

Population in need of further characterisation or Anticipated risk/consequence of the missing information

2.2.2. Proposed changes to Australia-specific safety concerns

This section can be used to request or record changes to Australia-specific safety concerns. If used, the section should follow the requirements for SVII.2 of the EU RMP (Rev 2):

<<Risk 1> previously classified as <important identified risk> <important potential risk> <missing information> is to be reclassified as <important identified risk> <important potential risk> <missing information> or <is removed from the list of safety concerns>>

Reasons for the reclassification or removal from the list of safety concerns:

<Changes in the level of scientific evidence for the causal association or risk-benefit impact>

For new proposals from the sponsor, discuss briefly the level of scientific evidence that has led to this re-classification/removal.

3. Pharmacovigilance plan

For biologicals, replace 'pharmacovigilance' with 'biovigilance' throughout the ASA.

3.1. Routine pharmacovigilance activities in Australia

Provide a brief summary or list of routine pharmacovigilance activities, beyond adverse reaction reporting and signal detection, that will be implemented in Australia, such as:

- specific adverse reaction follow-up forms
- enhanced passive surveillance
- observed vs expected analyses
- cumulative reviews of adverse events of interest

State clearly and justify any differences between routine activities described in the EU RMP and those proposed for Australia.

If there are Australia-specific safety concerns, describe the corresponding routine pharmacovigilance activities (beyond adverse reaction reporting and signal detection).

If specific adverse reaction follow-up forms are to be implemented, state whether the forms implemented in the EU (which should be included in Annex 4 of the EU RMP) will be used in Australia. If different forms are planned for use in Australia, attach them to the ASA.

If follow-up forms do not contain a field for recording Aboriginal and Torres Strait Islander ethnicity, describe how you will seek this information.

For biologicals, a detailed description of the biovigilance system in Australia should be provided, including:

- a summary of the sponsor's routine biovigilance activities
- details of the elements of the biovigilance system needed to support the additional biovigilance activities included in the RMP, and
- details of procedures for traceability of products from donor to recipient, and recipient to donor, to investigate and act on possible disease transmission.

3.2. Additional pharmacovigilance activities

State clearly and justify any differences between additional pharmacovigilance activities proposed in the EU RMP and those proposed for Australia. If all of the additional pharmacovigilance activities included in the EU RMP are considered to apply to Australia, state this.

3.2.1. Australia-specific additional pharmacovigilance activities

This section should:

- indicate whether there are additional pharmacovigilance activities for each Australia-specific safety concern, and
- provide the detail of any Australia-specific pharmacovigilance activities (which may be for Australia-specific safety concerns, or for safety concerns listed in the EU-RMP).

If there are no additional safety concerns for Australia or no Australia-specific pharmacovigilance activities for safety concerns listed in the EU-RMP then this can be simply stated.

Studies to evaluate the effectiveness of additional risk minimisation activities in Australia should be listed in Section 5.4.

For any additional pharmacovigilance activity that forms part of the Australian pharmacovigilance plan and is not described in the EU RMP, complete the summary using the format required in III.2 of the EU RMP, and provide the protocol in Annex 2 of the ASA, as shown below:

<PASS short name> summary

Study short name and title:

Rationale and study objectives:

Indicate the rationale for conducting the study (include also all the safety concerns addressed).

Present briefly the study objectives.

Study design:

State the study design. e.g. randomised clinical trial extension, observational chart-review, cohort study, self-controlled case series.

Study population:

Present briefly the population included in the study, in line with the inclusion and exclusion criteria.

Milestones:

Include all requested milestones for reporting to the TGA (e.g. protocol submission, interim reports, and final report submission) as well as major milestones from study protocol (e.g. start and end of data collection, interim progress reports, final study report completion, date of publication).

3.3. Summary table of additional pharmacovigilance activities

Provide a complete overview of the ongoing and planned additional pharmacovigilance activities for Australia, including those in the EU RMP and any further activities described in section 3.2.1 of the ASA.

Indicate whether TGA has required submission of any study protocols or reports and provide estimated dates.

The TGA does not routinely require submission of all clinical study reports from additional pharmacovigilance activities. Sponsors are expected to include information from additional pharmacovigilance activities in PSURs and update the RMP to reflect important new safety information as it emerges.

In some cases TGA may require submission of data from specific routine or additional pharmacovigilance activities, particularly for activities requested by the TGA. The timing of and method for submission of this data will be determined during the evaluation.

Sponsors must also comply with the pharmacovigilance reporting requirements in '[Pharmacovigilance responsibilities of medicines sponsors: Australian recommendations and requirements](#)'.

For each additional pharmacovigilance activity, state whether Australian patients are included.

Table 2: Ongoing and planned additional pharmacovigilance activities (example)

Study and status	Summary of objectives	Safety concerns addressed	Study location; Australian patients?	Submission to TGA*	
E.g. STUDY1 Planned	To evaluate...	Important potential risk 1	Multinational; yes	Required?	Deliverable and due date
E.g. Registry1 Planned	To evaluate risk of non-melanoma skin cancer in...	NMSC	Australia; yes	Yes	Annual report with each PSUR

*refers to requirement to submit clinical study protocols or reports as a condition of registration or to fulfil RMP commitments. Sponsors must also comply with the reporting requirements in ['Pharmacovigilance responsibilities of medicines sponsors: Australian recommendations and requirements'](#).

4. Clinical study plan for provisional registration

For applications for provisional registration, include an overview of the clinical study plan.

Attach the study protocols to the ASA, or provide a reference to the location of the protocols in another part of the eCTD dossier.

See the TGA Guidance '[Provisional registration process](#)' for further information and an example format for the clinical study plan overview.

5. Risk minimisation plan

5.1. Routine risk minimisation activities

This section should describe the routine risk minimisation used for each safety concern. You should provide a reference to the PI and CMI section and identify and justify any material differences between the statements in the SmPC and PL, and PI and CMI.

State whether the CMI will be included in the pack, and whether the pack will contain any other risk communication materials, such as a patient alert card, pack insert or instructions for use.

Table 3: Routine risk minimisation activities

Safety Concern	Routine risk minimisation activities	Differences between EU and Australian activities with justification
Important identified risks		
Risk 1	PI section: [e.g. 4.4]	

Safety Concern	Routine risk minimisation activities	Differences between EU and Australian activities with justification
	CMI section: [e.g. 'While you are taking [product]']	
	Other measures: [e.g. , pack size, package leaflet, warning statement on pack]	
Important potential risks		
Risk 2	PI section: [e.g. 4.4]	
	CMI section: [e.g. 'While you are taking [product]']	
	Other measures: [e.g. , pack size, package leaflet, warning statement on pack]	
Missing information		
Missing info 1	PI section: [e.g. 4.4]	
	CMI section: [e.g. 'While you are taking [product]']	
	Other measures: [e.g. , pack size, package leaflet, warning statement on pack]	

5.2. Additional risk minimisation activities

This section should describe the additional risk minimisation activities to be undertaken in Australia.

For **innovator medicines**, state clearly and justify any differences between additional risk minimisation activities planned for the EU and Australia. If you propose to implement all of the additional pharmacovigilance activities included in the EU RMP, state this.

For **generic or biosimilar medicines**, state clearly and justify any differences between additional risk minimisation activities conducted for the innovator medicine (if known) and your product.

<Removal of additional risk minimisation activities>

If you propose to remove an additional risk minimisation activity in Australia, you should provide a justification. The justification may refer to information provided in the EU RMP. If the justification relies on evidence presented in the EU RMP (such as from the evaluation of effectiveness of risk minimisation activities), you should provide a rationale for the applicability of the evidence in Australia and preferably using supporting evidence from Australia.

Rationale for the removal:

Include justification when an additional risk minimisation activity is proposed to be removed from the RMP.

5.2.1. Australia-specific additional risk minimisation activities

This section should:

- indicate whether there are additional risk minimisation activities for each Australia-specific safety concern, and
- provide the detail of any Australia-specific additional risk minimisation activities.

If there are no additional safety concerns for Australia and/or no Australia-specific risk minimisation activities for safety concerns listed in the EU-RMP then this can be simply stated.

For any additional risk minimisation activity that forms part of the Australian risk minimisation plan and is not described in the EU RMP, complete the summary below and provide draft key messages of the activity in Annex 3 of the ASA.

<Additional risk minimisation 1>

State type and/or title of risk minimisation activity

Objectives:

Include objectives including a list of risks addressed.

Rationale for the additional risk minimisation activity:

Include justification on why the particular additional risk minimisation is considered needed.

5.3. How additional risk minimisation activities will be implemented in Australia

Provide a table describing the implementation of all planned additional risk minimisation measures for Australia, including:

- the target audience for each activity
- how it will be implemented (including how materials will be disseminated)
- anticipated timeframes for implementation (such as expected start date for activity/dissemination and frequency of repetition, if relevant)

If it is not possible to include all relevant details in the table (e.g. for more complex additional risk minimisation activities such as controlled access programs), provide additional information in Annex 3 of the ASA.

Provide copies of draft Australian educational materials in Annex 3. Materials should be provided with content and intended layout, including images and graphic presentations of information. For digital additional risk minimisation tools, provide content and images of the on-screen layout of the information, and/or the login details or access codes to enable the TGA to evaluate the safety content in the format in which it is provided to the end user.

Table 4: Australian implementation of additional risk minimisation activities (example)

Additional risk minimisation activity	Target audience	Implementation details, including method(s) of dissemination	Time-points for and frequency of dissemination
<i>e.g. health professional guide and checklist</i>	<i>GPs pharmacists</i>	<i>Paper copies posted to GPs and pharmacists on sponsor-held mailing list</i>	<i>At launch</i> <i>Mailing list reviewed every 6 months and brochure mailed to new additions</i> <i>Repeat mail at 18 months after launch</i>
<i>e.g. patient guide</i>	<i>patients</i>	<i>Paper copies posted to GPs to provide to patients (initial mailing of 5 copies); GPs can re-order through sales reps and Medical Information</i> <i>Electronic copies available through patient support program website</i>	<i>At launch</i> <i>Mailing list reviewed every 6 months and brochure mailed to new additions</i> <i>Repeat mail at 18 months after launch</i>

5.4. How additional risk minimisation activities will be evaluated in Australia

Describe the evaluation of each additional risk minimisation activity to be conducted in Australia, including:

- how and when each activity will be evaluated
- how and when evaluation results will be reported to the TGA

You must demonstrate that your risk minimisation programme has been implemented as planned and is effective, and if not, what actions will be taken to improve effectiveness. Your plan(s) to measure effectiveness should include a clear description of what defines success prior to implementation.

In your evaluation plan you should consider the use of both process and outcome indicators.

Process indicators include measures of:

- reaching the target population
- assessing clinical knowledge
- assessing clinical actions

Outcome indicators are measures of:

- the safety outcome of the risk minimisation programme, such as the frequency and/or severity of adverse reactions

Methods to measure the effectiveness of risk minimisation activities should be proportionate to the risks being minimised.

If you propose to use an evaluation conducted in another market to contribute to the evaluation of activities in Australia, you should provide a justification for the applicability of this information. Consider any differences between the interventions implemented in Australia and Europe, and factors that may influence clinical knowledge or actions such as differences in the target audience, local guidelines, and reimbursement constraints. If we accept process indicators from other markets, we will usually also require evidence of effective implementation of the intervention(s) in Australia.

Refer to Guideline on good pharmacovigilance practices ([\(GVP\):Module XVI– Risk minimisation measures: selection of tools and effectiveness indicators \(Rev 2\)](#) for further detail about developing an evaluation plan.

The timeframes for reporting the outcomes of studies evaluating the effectiveness of risk minimisation activities will be determined during the evaluation process.

To assist you to record a specific, measurable and time-bound evaluation plan for your risk minimisation activities, we suggest you use the following table format. Protocols for evaluation activities should be attached to the ASA.

Table 5: Evaluation of additional risk minimisation activities (example)

Additional risk minimisation activity	Evaluation plan and criteria for success	Submission of results to TGA: deliverable and timeframe
<i>e.g. Health professional guide and checklist</i>	<p><i>Initial and 2nd distribution completed to at least 90% of target audience</i></p> <p><i>EU survey of GP and pharmacist knowledge, criteria as per protocol in EU RMP</i></p> <p><i>Australian drug utilisation study using GP prescribing data (see attached protocol)</i></p>	<p><i>Evaluation report (incl PASS results, DUS outcomes and distribution information) to be submitted to TGA by 24 months after first supply</i></p>
<i>e.g. Patient guide</i>	<p><i>Guide tested with consumers prior to finalisation and distribution</i></p> <p><i>Initial and 2nd distribution to GPs completed</i></p>	<p><i>Final materials provided for TGA review with results of testing, prior to distribution</i></p> <p><i>Distribution information to be included in evaluation report to be submitted to TGA by 24 months after first supply</i></p>

6. Summary of the RMP in Australia

Include a tabulated version of the summary of safety concerns for Australia (including the EU RMP summary of safety concerns and any Australia-specific safety concerns), and the associated routine and additional activities relevant to Australia.

- for pharmacovigilance activities, the activities relevant to Australia can include both local and international activities.
- for risk minimisation activities, only activities being conducted in Australia should be listed.

Australia-specific safety concerns should be indicated with an asterisk (*). We recommend that you use the table format below.

Table 6: Summary of the RMP in Australia (example)

Important Risks and Missing Information Safety concern		Routine pharmacovigilance activities†	Additional Pharmacovigilance Activities^	Routine risk minimisation activities	Additional Risk Minimisation Activities#
Important identified risks	<i>Hepatotoxicity</i>	<i>Targeted follow-up</i>	<i>None</i>	<i>Yes</i>	<i>HCP education</i>
	...				
Important potential risks	<i>Medication error</i>	<i>Targeted follow-up</i>	<i>EU patient registry</i>	<i>Yes</i>	<i>Dosing card; Patient alert card</i>
	<i>QT prolongation</i>		<i>Clinical Trial ##### (includes Australian patients)</i>		<i>None</i>
	...				
Missing information	<i>Use in pregnancy</i>		<i>EU patient registry</i>	<i>Yes</i>	<i>None</i>
	<i>Use in children</i>		<i>None</i>	<i>Yes</i>	<i>None</i>
	...				

† only include routine pharmacovigilance beyond adverse reaction reporting and signal detection

^ = All pharmacovigilance activities relevant to Australia should be listed, including those conducted overseas where the outcomes will be generalisable to Australian patients.

= Only additional risk minimisation activities that will be conducted in Australia should be included in the table.

7. References

Annexes

ANNEX 1. Follow-up forms to be implemented in Australia

ANNEX 2. Study protocols for planned Australian pharmacovigilance studies

ANNEX 3. Additional risk minimisation materials

Include draft versions for new submissions.

Include the key message(s) for additional risk minimisation materials if key messages are not included in the EU RMP.

Include protocols for any studies to assess the effectiveness of additional risk minimisation activities (if not attached to the EU RMP).

Contact information

Please direct any questions and advice relating to RMPs to:

Method	Contact
Post	RMP Coordinator Pharmacovigilance and Special Access Branch PO Box 100 Woden ACT 2606 Australia
Phone	02 6232 8390
Email	rmp.coordinator@health.gov.au

Version history

Version	Description of change	Author	Effective date
V1.0	Original Publication	Risk Management Plans Section/Office of Product Review	03/09/2012
V1.1	Updated Template	Risk Management Plans Section/Office of Product Review	05/09/2012
V1.2	Updated content	Risk Management Plans Section/Office of Product Review	14/09/2012
V1.3	Updated content	Risk Management Plans Section/Office of Product Review	03/10/2012
V2.0	Updated content, added Australian-specific annex as attachment	Risk Management Plan Evaluation Section/Post-market Surveillance Branch	May 2015
V3.0	Published for consultation – updated content to include reference to biologicals	Risk Management Plan Evaluation Section	October 2016
V3.1	Revised with biologicals content following consultation	Risk Management Plan Evaluation Section	November 2017
V3.2	Revised and circulated for targeted external consultation with new content re RMP compliance, generics, post-approval updates, new ASA, PSUR conditions	Risk Management Plan Evaluation Section	April 2018
V3.3	Revised following consultation	Risk Management Plan Evaluation Section	March 2019

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