Risk Management

Dr Iga Policinska

Principal Evaluator – Risk Minimisation Plan Evaluation Team

Department of Health and Aged Care, TGA

Agenda

Risk Management Principles

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Principles of risk management for medicines

- Benefit Outweighs the Risk
- Risk Management Plans
- Additional Risk Minimisation Activities

Risk Minimisation Measures

Risk minimisation measures are interventions intended to prevent or reduce the occurrence of adverse reactions associated with the exposure to a medicine, or to reduce their severity or impact on the patient should adverse reactions occur.

- Identification
- Characterisation
- Prevention
- Minimisation of risks

What is a Risk Management Plan?

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

- 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.

https://www.tga.gov.au/resources/resource/guidance/risk-management-plans-medicines-and-biologicals

What is an Australia Specific Annex?

- Submitted alongside the EU-RMP
- Documents the difference between the plan for Australia and the EU-RMP
- Documents differences in safety concerns between the EU and Australia and ensure that these are taken into account in determining an adequate risk management system
- Documents risk management activities not reflected in the EU RMP that are required to adequately address the safety concerns in Australia
- Documents differences in routine risk minimisation
- Record details of the dissemination and evaluation of effectiveness of risk minimisation activities in Australia
- Records milestones and timelines for reporting on additional pharmacovigilance and risk minimisation activities to the TGA

Evaluation of Risk Management Plans

Who is responsible for evaluating the RMP/ASA at the TGA?

What is considered in the evaluation?

- Summary of safety concerns
- Identification of additional safety concerns by other areas of the TGA
- Proposed product vigilance and risk minimisation activities

Risk Minimisation Activities

Routine minimisation activities

- Product Information
- Consumer Medicine Information
- Pack Size
- Packaging and labelling
- Medicine Scheduling

Safety concerns

- Frequency
- Seriousness
- Severity
- Impact on public health and
- Preventability

Electronic Medicines Compendium - https://www.medicines.org.uk/emc

Examples of Additional Risk Minimisation Activities

- Educational programs or tools for health professionals and/or consumers
- Controlled access programs
- Pregnancy prevention programs
- Direct healthcare professional communication

Effective Additional Risk Minimisation

- Tools
  - They require a clear objective to minimise the risk and optimise the risk-benefit balance.

- Stakeholders
  - Sponsors
  - Patients
  - Healthcare professionals

- Evolving area

Effectiveness of risk minimisation activities

- Evaluating the effectiveness of additional risk minimisation measures is necessary to establish whether an intervention has been effective or not, and if not why and which corrective actions are necessary.

- The evaluation should be performed for the additional risk minimisation tools individually and for a risk minimisation program as a whole.

Effectiveness evaluation should address different aspects of the risk minimisation:

- The process
- The impact
- The outcome

Evaluation of Effectiveness

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

Inclusion of aRMMs in the ASA

Rationale: When additional risk minimisation measure(s) are introduced a rationale should be provided for those additional measures;

Objectives: Each proposed additional risk minimisation measure(s) should include defined objective(s) and a clear description of how and which safety concern is addressed with the proposed additional risk minimisation measure(s);

Description: This section should describe the selected additional risk minimisation measures, including tools that will be used and key elements of content;

Implementation: This section should provide a detailed proposal for the implementation of additional risk minimisation measures (e.g. setting and timing or frequency of intervention, details of the target audience, plan for the distribution of educational tools; how the action will be coordinated where more than one marketing authorisation holder is involved);

Evaluation: This section of the RMP should provide a detailed plan with milestones for evaluating the effectiveness of additional risk minimisation measures in process terms and in terms of overall health outcome measures (e.g. reduction of risk).

How additional risk minimisation activities are evaluated in Australia

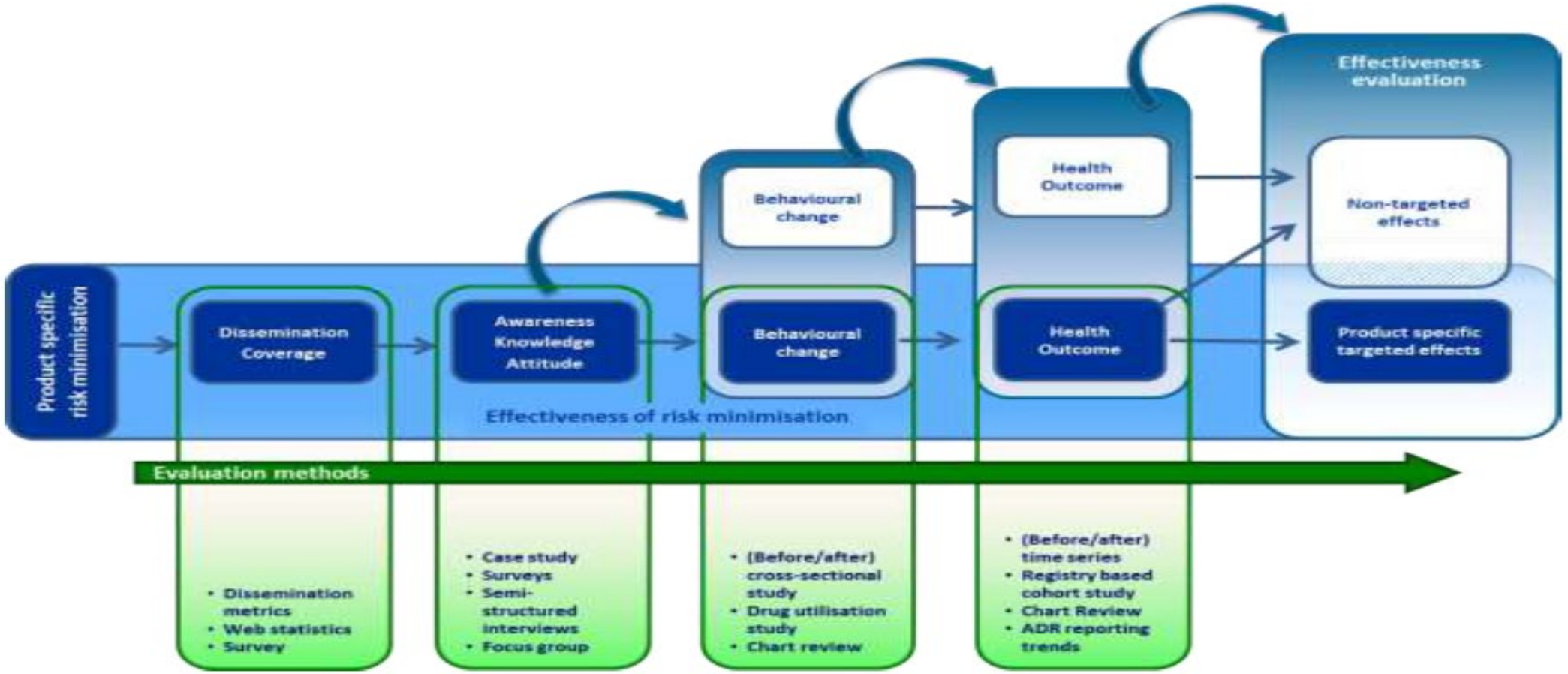
Describe the evaluation of each additional risk minimisation activity to be conducted in Australia, including:

- 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.



https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/pharmacovigilance-post-authorisation/good-pharmacovigilance-practices-gvp

EMA Guidelines adopted by the TGA

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

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.

Timeframe

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.

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 recommended that the updated RMP/ASA is submitted within **3 months** of the change being accepted by the EMA.

If you are not sure – contact us

Compliance with RMP commitments

You are responsible for:

- maintaining the currency of your ASA/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
- notifying the TGA of important changes to your RMP

Common RMP related findings in Pharmacovigilance Inspections

Deficiencies identified in this topic area included:

- Failure to access all approval letters and section 28 letters applicable to products on the ARTG and implement a process to verify ongoing compliance with the conditions imposed
- Failure to produce records to verify fulfillment of post-approval commitments.
- Delays in Periodic Safety Update Report (PSUR) submission
- Failure to implement the correct reporting period and/or submission frequency of Periodic Safety Update Reports (PSURs)
- Failure to notify, or delayed notification to, the TGA of the commencement of supply
- Delays in the submission of an updated Risk Management Plan (RMP) / Australian Specific Annex (ASA) to the TGA
- Failure to notify the TGA regarding an intended significant change to the RMP-ASA (e.g. cessation of an additional risk minimisation activity) before the change was implemented.

Website and link references

RMP Guidance	https://www.tga.gov.au/resources/resource/guidance/risk-management-plans-medicines-and-biologicals
Pharmacovigilance – Responsibilities	https://www.tga.gov.au/resources/resource/guidance/pharmacovigilance-responsibilities-medicine-sponsors
Pharmacovigilance Inspections	https://www.tga.gov.au/resources/resource/guidance/pharmacovigilance-inspection-program-guidance-medicine-sponsors
European Medicines Agency (EMA)	https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/pharmacovigilance-post-authorisation/good-pharmacovigilance-practices-gvp
Electronic Medicines Compendium (EMC)	https://www.medicines.org.uk/emc/browse-medicines

Therapeutic Goods Administration (TGA)

Exhibition booth **No.1**

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rmp.coordinator@health.gov.au

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www.tga.gov.au

Australian Government

Department of Health and Aged Care

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