About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health, and is responsible for regulating medicines and medical devices.

- The TGA administers the Therapeutic Goods Act 1989 (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance), when necessary.

- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines and medical devices.

- The TGA relies on the public, healthcare professionals and industry to report problems with medicines or medical devices. TGA investigates reports received by it to determine any necessary regulatory action.

- To report a problem with a medicine or medical device, please see the information on the TGA website <https://www.tga.gov.au>.
## Version history

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Introduction

The Therapeutic Goods Administration (TGA) administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance).

The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines, vaccines, medical devices and biologicals. The TGA considers the benefit-risk balance for the intended population that the therapeutic product is to be used in.

The benefit-risk balance for the individual is a decision usually made by health professionals in consultation with each patient and takes into account additional factors such as previous treatment, disease severity, alternative therapeutic products/treatment options and patient preferences.

Once a therapeutic product is approved, the TGA continues to monitor the product in the market through therapeutic product vigilance activities.

This document outlines Australia’s therapeutic product vigilance processes.

1.1 TGA’s approach to therapeutic product vigilance

The aim of therapeutic product vigilance is to continually monitor and evaluate the safety and efficacy (performance) profile of therapeutic products and to manage any risks associated with individual products.

The TGA’s approach to therapeutic product vigilance is guided by the following principles:

- **i. Communication of safety information to the public**
  Therapeutic product vigilance should provide a mechanism for involving consumers and health professionals in the provision and the appropriate use of safety information related to therapeutic products in Australia.

- **ii. Uphold product efficacy and safety standards**
  The requirement for specific vigilance activities will be for the purpose of protecting the health and safety of Australians and will in no way result in the reduction in a product’s requisite efficacy and safety.

- **iii. Adopt a product lifecycle approach**
  It is well recognised that therapeutic product vigilance needs to occur throughout a product’s lifecycle to take into account the entire body of evidence that accumulates throughout the lifecycle of the product.

- **iv. Align with international best practices and standards**
  The TGA has committed to aligning its regulatory approaches related to therapeutic product vigilance, wherever possible, with those of comparable international regulatory counterparts. This includes a commitment to the integration of internationally harmonised vigilance tools which provides the vehicle through which international work and information sharing can proceed.
v. Facilitate industry compliance with vigilance best practices
   
   The TGA will provide regulated parties with guidelines to follow vigilance best practices.

vi. Align with the TGA’s decision-making framework
   
   Therapeutic product vigilance activities are guided by two key components: transparency and timely decision-making; and meaningful public involvement.

vii. Continuously improve therapeutic product vigilance
   
   The TGA recognises that therapeutic product vigilance activities may change over time as knowledge of a product evolves. A product’s vigilance requirements should be subject to reconsideration over its lifecycle, on the basis of the evolution of knowledge, technology and society's expectations. Also, therapeutic product vigilance tools will be evaluated for effectiveness in carrying out their desired purposes.

Shared responsibilities for therapeutic product vigilance

The maintenance and improvement of health and safety is a shared responsibility. In addition to government and regulated industry, health professionals, patients, consumers and their respective associations play an important role in reporting therapeutic product safety-related issues.

2.1 Sponsors

Sponsors have the primary responsibility for the safety of any therapeutic products they import, supply or export from Australia. Sponsors must comply with legislative requirements for therapeutic product vigilance under the Act and there are applicable offences and penalties for not complying. The legislative requirements for therapeutic product vigilance vary depending on the type of therapeutic good.

Further information on the legislative requirements for sponsors is available in the Australian Guideline for Pharmacovigilance Responsibilities of Sponsors of Medicines (AGPRSM), Australian Regulatory Guidelines for Medical Devices (ARGMD) (Part 3-Post-market) and Australian Regulatory Guidelines for Biologicals (ARGB).

2.2 TGA

The TGA maintains up-to-date safety information on therapeutic products that is communicated through a variety of means to health professionals, patients and consumers. The TGA is committed to advancing public health through the market authorisation of beneficial, innovative therapeutic products and by providing timely, evidence-based and authoritative information to allow consumers and health professionals to make informed decisions.

The TGA is responsible for taking appropriate action, when necessary, regarding the maintenance, amendment, suspension or cancellation of product registration, listing or inclusion in the Australian Register of Therapeutic Goods (ARTG). The TGA is also responsible for operating Australia’s therapeutic product vigilance system, ensuring that methods are in place to receive and manage vigilance data, monitor and evaluate that data, and manage the risks.
2.3 Health professionals, patients and consumers

Health professionals, patients and consumers are encouraged to inform the TGA of any problems they encounter (hazards, adverse events, malfunctions, and non-compliance) with regulated therapeutic products throughout their lifecycle, including products used in a clinical trial setting. Information on how to report problems to the TGA can be found at 'Report a problem'.

Australia’s therapeutic product vigilance system

The TGA seeks to promote high standards of therapeutic product vigilance for the protection of the health and safety of Australians, and to facilitate access to products vital to the health and wellbeing of all Australians through a 'lifecycle approach' to product monitoring and vigilance. The lifecycle approach recognises that clinical trial data used to evaluate a therapeutic product for entry on the ARTG is limited and that real-world experience can identify previously unknown safety and efficacy information such as interactions between drugs, between a drug and a medical device or between a medical device and a biological, and provide information about rare and uncommon adverse events.

The TGA’s product vigilance system consists of an integrated set of product vigilance tools that work together to protect the health and safety of Australians. This includes tools for information collection, monitoring, evaluation, and risk management from the development stage through to initial marketing and continued supply of a therapeutic product in Australia.

The TGA is working towards integration of internationally harmonised vigilance tools that will strengthen the current system and facilitate international work sharing and information sharing arrangements.

![Product Vigilance and Benefit-Risk Management Cycle](image)

3.1 Product vigilance tools

Product vigilance (PV) tools are defined by the World Health Organisation (WHO) as tools used to detect, assess, understand or prevent adverse events or any other health product-related problems. For the purpose of the TGA, therapeutic product vigilance tools are defined as tools designed to facilitate the collection and evaluation of information pertaining to the benefits and risks associated with the use of therapeutic products. A description of the product vigilance tools in use or in development is found in Table 1.

Table 1 – Description of Product Vigilance Tools

<table>
<thead>
<tr>
<th>PV Tool</th>
<th>Description of Method</th>
<th>Product Lines</th>
<th>Primary Source of Information</th>
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<tbody>
<tr>
<td>Risk management plan (RMP)</td>
<td>Summary of the known important safety information about the therapeutic product (safety specifications). Plans to identify and characterise known or potential safety concerns (pharmacovigilance plan) and to minimise any identified or potential safety risk (risk minimisation plan). High-risk medicines may require an assessment of benefit.</td>
<td>Registered medicines</td>
<td>Sponsors</td>
</tr>
<tr>
<td>Adverse event (AE) reporting</td>
<td>Reports on harmful and unintended responses to medicines, vaccines, biologicals and medical devices marketed in Australia or in clinical trials. Expedited reporting of serious unexpected clinical trials adverse events. Reports regarding deficiencies in labelling, instructions or packaging, defective components, performance failures, poor construction or design of medical devices marketed in Australia.</td>
<td>Listed medicines Registered medicines and vaccines Biologicals Medical devices</td>
<td>Sponsors, health professionals, patients, consumers and clinical trial sponsors</td>
</tr>
</tbody>
</table>
### PV Tool Description of Method Product Lines Primary Source of Information

<table>
<thead>
<tr>
<th>Periodic Safety Update Report (PSUR)/Periodic Benefit-Risk Evaluation Report (PBRER)</th>
<th>A comprehensive and critical analysis of new or emerging information on the risks of the product, and, where pertinent, on its benefit in approved indications, to enable an appraisal of the product’s overall benefit-risk profile.</th>
<th>Registered medicines</th>
<th>Sponsors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual reports for medical devices</td>
<td>A periodic comprehensive assessment of the worldwide complaint data of a medical device.</td>
<td>Medical devices classified as AIMD, Class III and implantable Class IIb</td>
<td>Sponsors</td>
</tr>
<tr>
<td>Pharmacovigilance inspections (proposed)</td>
<td>Inspection of a manufacturer’s records of adverse events and reporting to the TGA. A medical device manufacturer’s adverse event records are inspected as part of the Quality Management System (QMS) assessment.</td>
<td>Listed medicines Registered medicines and vaccines Biologics Medical devices</td>
<td>Sponsors, manufacturers</td>
</tr>
<tr>
<td>Environmental scanning</td>
<td>Collection and review of scientific and medical literature, media reports and regulatory news to identify safety issues that require further investigation.</td>
<td>Listed medicines Registered medicines and vaccines Biologics Medical devices</td>
<td>Media, academia, governments, industry and consumers</td>
</tr>
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#### 3.2 Prioritisation and benefit-risk assessment

With the increased volume of signals being identified by the TGA, a risk-based process has been developed for the screening and prioritisation of signal investigations being undertaken. This process provides a solid and consistent rationale for allocation of resources towards the most urgent issues and ensures that the TGA can respond appropriately and in a timely manner to emergent safety issues. However, all identified issues are recorded and acted upon within a timeframe appropriate to their impact on public health. As outlined in Table 2, there may be different requirements for a new product where there is limited information for real world usage. The different product vigilance tools use prioritisation matrices as guides for the request and processing of safety and effectiveness information submitted to or gathered by the TGA.
Table 2 – Product vigilance tool prioritisation schemes

<table>
<thead>
<tr>
<th>PV Tool</th>
<th>Description of prioritisation scheme</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse event reporting</td>
<td>Adverse event reports have an initial risk assessment and a priority level is determined. Serious reports are reviewed and addressed as soon as possible by the TGA.</td>
<td>All adverse event reports follow an electronic workflow process with priority reports having the most stringent timelines.</td>
</tr>
<tr>
<td></td>
<td>The TGA applies a causality rating for the adverse event and in some cases requests further clinical or laboratory information from the reporter to allow causality to be assessed.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medical officers review serious reports and TGA staff regularly analyse reporting data using internationally recognised methodology such as proportional reporting ratio (PRR) to detect trends and clusters.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For medical devices a panel of scientific, engineering and clinical experts assesses all reports. This panel determines what level of investigation will take place.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-serious reports are used for trending purposes.</td>
<td></td>
</tr>
<tr>
<td>PV Tool</td>
<td>Description of prioritisation scheme</td>
<td>Comment</td>
</tr>
<tr>
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</table>
| RMP     | Prioritisation is based on levels of risk or uncertainty – products we know little about (high level of uncertainty) and those that are known to have significant risk. The following applications for registration will require a RMP:  
- applications for a new chemical entity  
- applications for a new Class 3 or 4 biological  
- applications for a significant extension of indications  
- extension to a paediatric population  
- applications to change the registration of a drug, where the change will result in different dosage forms, a change in the treatment population or a change in the safety profile of the drug. | The TGA can request a RMP be submitted for therapeutic goods that are already approved and on the ARTG when a safety issue arises.  
Sponsors are encouraged to review the European Union (EU) Guideline on Risk Management Systems for Medicinal Products for Human Use (EMEA/CHMP/96268/2005), which outlines when a RMP is required. |
| PSUR/PBRER | Prioritisation is based on levels of risk or uncertainty – products we know little about (high level of uncertainty) and those that are known to have significant risk and is dependent on the RMP process. | The prioritisation scheme aligns with the RMP process.  
Higher risks could result in more frequent reporting. |
| Annual reporting for medical devices | High-risk medical devices that are new to the Australian market are monitored for seriousness of adverse event reports and complaints. | Review of data may trigger further investigation or additional conditions of inclusion on the ARTG or other regulatory action. |

Therapeutic product vigilance evaluation involves the ongoing assessment of the benefits and risks of a product (including data from adverse event reports, clinical trials, meta-analysis, observational studies, etc.) and the assurance that benefits outweigh the risks for a given population during clinical trials and following its entry in the ARTG. The TGA has developed an approach to a benefit-risk assessment based on consultation with international regulators and other relevant agencies.

Benefit-risk assessment is an important regulatory tool that highlights the benefits and risks of therapeutic products. Industry may be responsible for developing benefit-risk assessments in some cases and the TGA’s responsibility is to evaluate these documents and other relevant information when a change in the product’s benefit-risk profile is identified.
The TGA uses both qualitative and quantitative methodologies when performing benefit-risk assessment reviews and also engages collaboratively with international stakeholders such as the Council for International Organizations of Medical Sciences (CIOMS) and other regulators to refine these methodologies.

The TGA may seek advice from the Advisory Committee on the Safety of Medicines (ACSM), the Advisory Committee on the Safety of Vaccines (ACSOV) and the Advisory Committee on the Safety of Medical Devices (ACSMD) on the safety, risk assessment, risk management, effectiveness and performance of relevant therapeutic goods. The Orthopaedic Subcommittee is a group of independent orthopaedic surgeons who provide expert advice to the ACSMD and the TGA on the safety, quality and performance of orthopaedic devices.

### 3.3 Communicating vigilance activities

The TGA communicates its monitoring and evaluation of information related to the safety and efficacy of marketed therapeutic products through a variety of means.

The TGA publishes Australian Public Assessment Reports (AusPARs) which outline our evaluation of recently registered prescription medicines, including important efficacy and safety information. In addition, the TGA publishes the Product Information (PI) and Consumer Medicine Information (CMI) for prescription and some non-prescription medicines.

Information is shared with the public and with health professionals through safety alerts published on the TGA’s website and the bimonthly Medicines Safety Update (MSU) and Medical Devices Safety Update (MDSU). The TGA has also established an early warning communication system to advise of potential safety issues for medicines and medical devices.

Information in the publicly searchable Database of Adverse Event Notifications (DAEN) comes from reports made to the TGA by a wide range of sources, including sponsors, health professionals and consumers. Reports received by the TGA up until three months prior to the date of access are available from the database. The TGA uses this three-month period to investigate each adverse event report.

The System for Australian Recall Actions (SARA) provides consumers, health professionals, sponsors, wholesalers, hospitals and retailers with access to information about recall actions occurring in Australia for therapeutic goods. The database holds information on recall actions that have been undertaken in Australia since 1 July 2012.

The TGA shares vigilance data with state and territory health departments and other partners such as the National Centre for Immunisation Research and Surveillance (NCIRS) and also provides adverse event information to the WHO and overseas regulatory agencies.

### 3.4 Practical aspects of the product vigilance system

The TGA takes into consideration the best practices on various aspects of an integrated product vigilance system. Although it is important to align as much as possible with international product vigilance best practices, the TGA will have consideration of the impacts on safety, as well as the administrative burden on both the sponsor and the regulator when deciding on steps forward for implementing product vigilance requirements.
Annex 1 - Acronyms and abbreviations

AE  Adverse Event
AIMD  Active Implantable Medical Device
AGPRSM  Australian Guideline for Pharmacovigilance Responsibilities of Sponsors of Medicines
ACSMD  Advisory Committee on the Safety of Medical Devices
ACSOM  Advisory Committee on the Safety of Medicines
ACSOV  Advisory Committee on the Safety of Vaccines
ARGB  Australian Regulatory Guidelines for Biologicals
ARGMD  Australian Regulatory Guidelines for Medical Devices
ARTG  Australian Register of Therapeutic Goods
AusPAR  Australian Public Assessment Report
CIOMS  Council for International Organisations of Medical Sciences
CMI  Consumer Medicine Information
EU  European Union
MDSU  Medical Devices Safety Update
MSU  Medicines Safety Update
OSC  Orthopaedic Sub-committee
PBRER  Periodic Benefit-risk Evaluation Report
PI  Product Information
PRR  Proportional Reporting Ratio
PSUR  Periodic Safety Update Report
PV  Product Vigilance
RMP  Risk Management Plan
the Act  Therapeutic Goods Act (1989)
TGA  Therapeutic Goods Administration
WHO  World Health Organization