



Australian Government

Department of Health and Ageing
Therapeutic Goods Administration

Trans-Tasman early warning system

Processes in Australia and New Zealand

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TGA Health Safety
Regulation

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About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health and Ageing, 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 <<http://www.tga.gov.au>>.

About Medsafe

- Medsafe is the New Zealand Medicines and Medical Devices Safety Authority and is responsible for the regulation of therapeutic products in New Zealand through administration of the *Medicines Act 1981*.
- Medsafe is a business unit of the New Zealand Ministry of Health.
- Medsafe's Mission is: 'To enhance the health of New Zealanders by regulating medicines and medical devices to maximise safety and benefit.'
- In working to achieve the stated mission Medsafe:
 - applies accepted international practice to the regulation of therapeutic products
 - provides efficient services measured against agreed stated performance indicators
 - prepares and maintains regulatory guidelines reflecting sound science and promoting evidence based decisions
 - applies processes that are consistent, transparent and minimise the costs of regulatory action
 - provides timely and unbiased information to health professionals and consumers about the safe use of therapeutic products.

To find out more about medicines regulation in New Zealand please see the information on the Medsafe website at <<http://www.medsafe.govt.nz>>.

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Overview of the Early Warning System

The Therapeutic Goods Administration (TGA) and the New Zealand Medicines and Medical Devices Safety Authority (Medsafe) have established parallel early warning systems in Australia and New Zealand for advising of potential safety concerns associated with medicines or medical devices.

The TGA and Medsafe will apply an agreed communication process independently to potential safety concerns identified with therapeutic products through their existing therapeutic product vigilance processes. These communications will be country specific and may differ reflecting different legislative requirements, and different availability and/or usage of certain therapeutic products between Australia and New Zealand.

The key principles of the early warning system are:

Timely	This will be achieved by prioritisation of safety concerns and prompt assessment and communication of these concerns (where required) during the normal vigilance process.
Sustainable	The process, procedures and thresholds for communication have been designed to ensure the scheme will be sustainable by the TGA and Medsafe.
Responsive	The scheme will identify and communicate safety concerns relevant to stakeholders and incorporate stakeholder feedback
Engaging	The scheme will provide useful advice targeted for different stakeholders

There are two types of communications that can be issued as part of the Early Warning System.

1. Monitoring communications

These are early communications about potential safety concerns which have not been fully investigated. The intention of these communications is to highlight potential safety concerns that have been identified by the TGA or Medsafe and to encourage further reporting.

The decision to issue a monitoring communication can be made either at:

- the initial assessment/risk analysis step when all safety concerns are considered and may be communicated; or
- the signal investigation/assessment step when concerns deemed to be safety signals are considered and may be communicated.

2. Alert communications

An alert communication is issued once a safety concern has been investigated. Alerts contain more information on the safety concern and provide advice on actions that may need to be taken by health professionals and consumers.

This document outlines the processes involved in the trans-Tasman early warning system.

Monitoring communications

Decision criteria - initial assessment stage

Safety concerns with medicines and medical devices will be considered for a monitoring communication at the initial assessment/risk analysis step if they meet the following criteria:

The product is available in Australia and/or New Zealand.

Australia	Entered on the Australian Register of Therapeutic Goods (ARTG) .
New Zealand	Approved medicines can be found in Medsafe's product/application search . Certain unapproved medicines are funded by PHARMAC. Medical devices are contained in the WAND database.

Unapproved medicines are not considered for monitoring communications.

AND AT LEAST ONE OF THE FOLLOWING:

The potential safety concern could be serious by international standards and there may be insufficient information available to support a review at the time of the communication.

For medicines, the definition of serious according to the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) – Clinical safety data management: definitions and standards for expedited reporting (E2A) is:

- A **serious adverse event** or reaction is any untoward medical occurrence that at any dose results in death, is life threatening, requires inpatient hospitalisation or results in prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, is a congenital anomaly, is a medically important event or reaction.

For medical devices the definition used is an **adverse event** that has led to or might lead to:

- death to a patient, user or other person; or
- a serious injury or serious deterioration to a patient, user or other person, including
 - a life-threatening illness or injury
 - permanent impairment of a body function
 - permanent damage to a body structure
 - a condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

OR

There is or is likely to be interest in the potential safety concern from consumers, health professionals, government or media.

This will be determined though the volume and/or nature of enquiries received by the TGA and or Medsafe for the current concern or previous similar concerns. Enquires may come from consumers, media, health professionals or other government agencies.

OR

Advice from an Expert Advisory Committee.

The TGA and Medsafe have a number of statutory advisory committees from which independent expert advice on specific scientific and technical matters can be obtained. This advice assists with the TGA and Medsafe's regulatory decision making and other regulatory processes.

Decision criteria - signal investigation stage

Safety concerns with medicines and medical devices will be considered for a monitoring communication at the Signal Investigation stage if they meet the following criteria:

The product is available in Australia and/or New Zealand.

See definition above.

AND

Previously unknown safety concern or a significant change to the frequency of a known safety concern.

A concern is considered to be previously unknown if it is the first time the regulator has become aware of the concern i.e. a new concern which is not outlined in the product information for the therapeutic product.

A change in frequency is based on the previously reported frequency either from clinical trials (as outlined in the product information) or as previously estimated from reporting rates to the regulator.

AND

The source(s) are considered reliable.

Reliable sources include: spontaneous reports that meet the World Health Organization causality assessment of definite or probable for medicines, or spontaneous reports that meet the guidelines set out by the International Medical Device Regulators Forum for medical devices, other regulatory agency reports which include assessable data, peer-reviewed journal papers, unpublished data from sponsors where the study had an independent monitoring board or Periodic Safety Update Report (PSUR)/Periodic Benefit-Risk Evaluation Report (PBRER) special review topics, evidence of a safety concern provided by a member of a professional college.

AND

The regulator (TGA/Medsafe) is undertaking an investigation/assessment of the safety concern.

AND AT LEAST ONE OF THE FOLLOWING

The safety concern is serious by international standards.

See definition above.

OR

There is or could be significant interest in the safety concern from consumers, health professionals, government or media.

See definition above.

OR

Advice from an Expert Advisory Committee.

See definition above.

Content of monitoring communications

Following the decision to issue a monitoring communication, the communication will be drafted for publication on the TGA and/or Medsafe early warning system webpages.

Monitoring communications will include the following types of information.

Title	The name of the product involved (trade name and/or active ingredient) and a reference to the concern.
Publication date	The date the monitoring communication was published
Safety concern	A brief description of the concern including any specific rates or incidence figures, confounding factors and other useful details about the concern, e.g. if concern is only relevant in a particular patient group.
Product details	Outline of the products involved including applicable reference numbers, sponsor and manufacturer details, indications or intended purpose and/or efficacy/benefits
Relevant safety information	Brief safety information for consumers or health professionals in relation to the concern including providing appropriate links e.g. Consumer Medicine Information (CMI) or data sheet/Product Information (PI).
Regulator actions	Outline what the Regulator is doing in regards to the safety concern, e.g. is continuing to monitor reports and events relating to the concern, is investigating or will investigate the concern. Note if Medsafe/TGA are communicating a similar issue
How to report	Information on how to report adverse events
Outcome	A description of the outcome of the safety concern. This information may be provided within the original monitoring communication or as a link to a new monitoring communication, an alert communication and/or a recall action.

Publication of monitoring communications

The sponsor(s) of all relevant products will be provided with a copy of the communication. A copy of the communication will also be provided to the other regulator. Sponsors will be requested to point out any factual inaccuracies in the communications and any may also be requested to provide information about safety concerns which the regulator has decided require investigation (as per existing therapeutic product vigilance processes).

Once the communication has been approved it will be published on the regulators website. In order to balance the provision of information with the perception of information overload these communications will not be actively provided to stakeholders. However, stakeholders can subscribe to an RSS feed (Australia only) and/or email lists to receive notification of new monitoring communications published on the regulators website.

Alert communication

Decision criteria

Safety concerns with medicines and medical devices will be considered for an alert communication if they meet the following:

The safety concern has been assessed by the regulator (TGA/Medsafe).

This will be according to the normal therapeutic product vigilance procedures of TGA or Medsafe. Safety concerns with unapproved medicines are investigated if they affect significant numbers of consumers.

AND AT LEAST ONE OF THE FOLLOWING

The safety concern could be avoided by a behavioural change.

For example by not using the therapeutic product in a particular patient group.

OR

The safety concern could be detected prior to the use of the therapeutic product.

Medicines, these are detectable risk factors such as renal function that can be assessed before use. Medical devices, there is a system or diagnostic test that can determine if the medical device is faulty prior to use.

OR

There is or likely to be interest in the safety concern from consumers, health professionals, government or media.

See definition above.

OR

Advice from an Expert Advisory Committee.

See definition above.

Content of alert communications

Alert communications will include the following types of information.

Title	The name of the product involved (trade name and/or active ingredient) and a reference to the concern.
Publication date	The date the alert communication was published.
Safety concern	A brief description of the concern including any specific rates or incidence figures, confounding factors and other useful details about the concern, e.g. if concern is only relevant in a particular patient group.
Product details	Outline of the products involved including applicable reference numbers, sponsor and manufacturer details, indications or intended purpose and/or efficacy/benefits
Information for consumers and caregivers	Safety related information advising of actions or advice for consumers and caregivers.
Information for health professionals	Safety related information advising of actions or advice for health professionals including an outline of different actions for different groups (if required).
Summary and outcome of investigation	A summary of the investigation of the concern including an overview of the data assessed and an outline of the conclusions/outcomes from or in relation to the investigation.
How to report	Information on how to report adverse events.
Further information	Will include links (where applicable) to other useful sources of information, e.g. CMI, data sheet/ product information (PI) and/or parallel communications issued in Australia/New Zealand.

Publication of alert communications

The sponsor(s) of all relevant products will be provided with a copy of the communication. A copy of the communication will also be provided to the other regulator. Sponsors will be requested to point out any factual inaccuracies in the communications. The regulator will have collaborated with relevant sponsors during the investigation of the safety concern (as per existing therapeutic product vigilance processes).

Once the communication has been approved it will be published on the TGA and/or Medsafe websites. New alerts will be highlighted in the news section of the regulator's home page.

Dependent on the urgency and content of the alert communications, these will be actively shared with relevant stakeholders such as health professional and consumer organisations. Stakeholders can also subscribe to an RSS feed (Australia only) and/or email lists to receive notification of new alert communications published on the regulators website. Alert communications will also be linked into other electronic systems over time.

Updates to communications

All monitoring communications will have a subsequent communication advising the outcome of the safety concern. Alert communications may also be updated, although it is anticipated that in many cases the safety concern will be closed after the alert has been issued.

In addition follow up communication(s) may be issued after an initial monitoring communication and prior to a final communication. The need for follow up communications will be assessed on a case by case basis and will consider such factors as:

- the estimated length of time the signal investigation/assessment will take to complete
- time since the monitoring communication was issued
- the complexity of the material
- the level of public interest in the potential safety concern/signal
- feedback from consumers and/or health professionals on previous communications.

These communications will take the form of an alert communication, if they meet the defined criteria (described above). Otherwise an updated monitoring communication will be published. Related and updated communications regarding a safety concern will include appropriate links so users can easily identify the latest information issued on a safety concern.

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Reference/Publication #