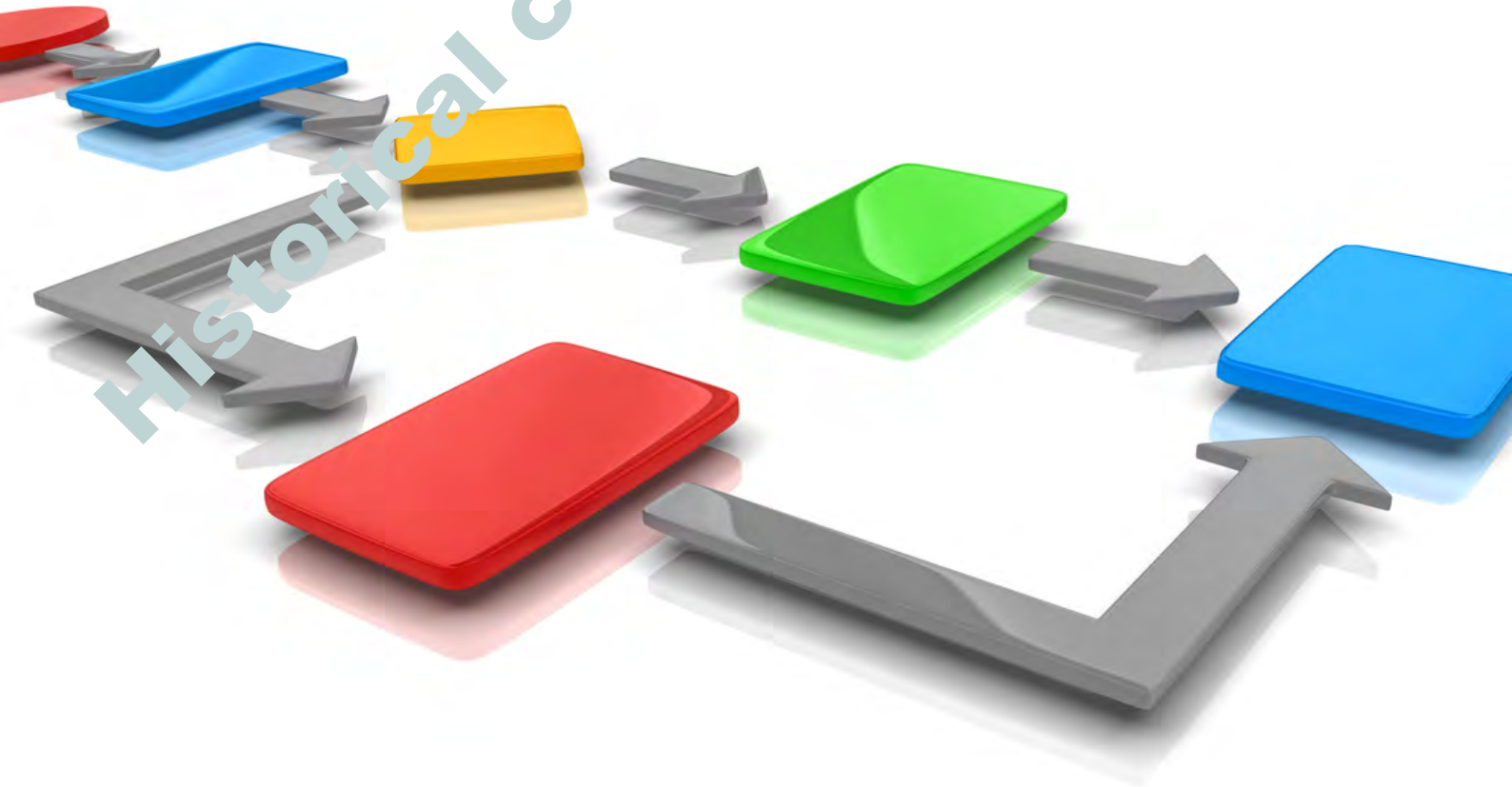
Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

MEDSAFE
NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY
A BUSINESS UNIT OF THE MINISTRY OF HEALTH

The Trans-Tasman early warning system

How the process will work in Australia and New Zealand

Version 1.0, March 2013



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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 wi the use of medicines and medical devices.
- The TGA relies on the public, healthcare professionals and industry to repo t p blems 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 se t t information on the TGA website <www.tga.gov.au>.

About Medsafe

- Medsafe is the New Zealand Medicines and Medical De ic s Safety Authority and is responsible for the regulation of therapeutic pro du in New Zealand through administration of the *Medicines Act 1981*.
- Medsafe is a business unit of the New Zea nd M nistry of Health.
- Medsafe's Mission is: 'To enhance the he h of New Zealanders by regulating medicines and medical devices to m in se safety and benefit.'
- In working to achieve the stated mis ion Medsafe:
  - applies accepted inter t nal practice to the regulation of therapeutic products
  - provides efficient se v s measured against agreed stated performance indicators
  - prepares and mai ins regulatory guidelines reflecting sound science and promoting ev ence based decisions
  - applies pr ss es that are consistent, transparent and minimise the costs of regula or action
  - pr v es timely and unbiased information to health professionals and consumers ab t the safe use of therapeutic products.

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

Contents

Background to the early warning system

The Prime Ministers of Australia and New Zealand agreed on 20 June 2011 to proceed with a joint scheme for the regulation of therapeutic products. The creation of a joint regulatory scheme across both countries will safeguard public health and safety, while encouraging economic integration and benefitting health professionals, consumers and industry in both countries.

A number of initial joint TGA/Medsafe projects have been agreed aimed at initiating the alignment of regulatory procedures. One of these business to business projects is to establish a trans-Tasman early warning system of potential safety concerns around therapeutic products. Further information about the formation of the Australia New Zealand Therapeutic Products Agency (ANZTPA) can be found on the TGA, Medsafe and transition to ANZTPA websites.

Introduction to the early warning system

The purpose of this business to business project between the TGA and Medsafe is:

- to establish a trans-Tasman early warning system for advising the public about potential safety concerns associated with medicines and medical devices.

As a first step in this project, the TGA and Medsafe consulted with the United States Food and Drug Administration (FDA), Health Canada and Health Singapore regarding their current alerting systems for medicines. The information provided by these regulators helped inform the background document produced for the jointly organised workshops with stakeholders held during April 2012. There were three workshops held in Melbourne, Sydney and Wellington which were attended by consumer, health professional, government and industry stakeholder representatives. The aim of these workshops was to gather opinions on what safety concerns should be included in an early warning system, and when and how these safety concerns should be communicated. The results of these workshops have been compiled and shared with participants. The final compilation document and workshop background document are available on the Medsafe , TGA and ANZTPA websites.

Medsafe has already trialled an early communication system called M². Information from this trial indicates that the publication of early communications can stimulate further reporting of adverse events. Actions have been taken as a result of these stimulated reports to improve medicine safety. For other concerns, which did not receive further reports, the lack of new reports assisted Medsafe's decision not to investigate the concern further.

The next stage of this project was to identify and agree on a process for the early warning system. To facilitate the development of the process, the TGA and Medsafe held a series of internal workshops and discussions in August 2012. The process described in this

document is based on the results of these joint discussions and the stakeholder workshops.

The scope of this project encompasses the creation of parallel communication systems in Australia and New Zealand that use the same process.

The TGA and Medsafe will apply the agreed communication process independently to potential safety issues 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.

Outside the scope of this project:

- The therapeutic product safety vigilance processes in Australia and New Zealand as outlined in Figure 1 below (grey boxes).
- The creation of a single integrated early warning system (this may be considered in the future).

Development of a monitoring communication scheme for therapeutic products new to the market. The TGA is undertaking a feasibility study into the development of an early post-marketing risk communication scheme for therapeutic goods with consideration of international models as part of the Blueprint reform program.

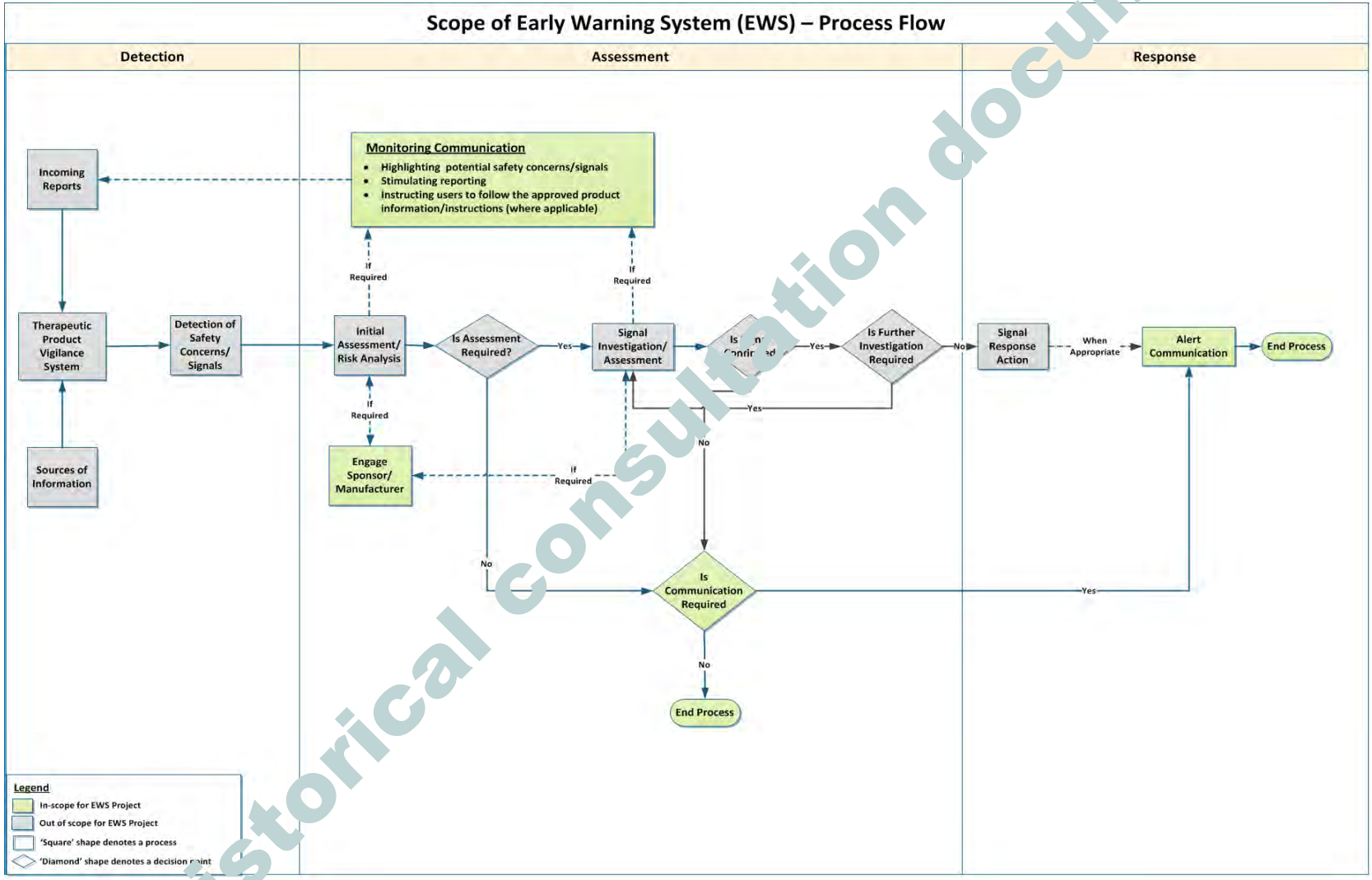
Overview of the early warning system

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.

The location of the early warning system in the overall therapeutic product vigilance process flow is outlined in Figure 1 below (green boxes);

Figure 1: Location of the early warning system in the therapeutic product process



There are several points in the therapeutic product vigilance process where the decision to issue a communication can be made. Two different types of communication are possible: monitoring communication and an alert communication.

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.

All the monitoring communications issued will have a subsequent communication advising the outcome of the safety concern. The decision to issue an alert communication is made at the conclusion of the signal investigation/assessment and is made independent of whether a monitoring communication was issued or not.

Follow up communication(s) may be issued after a monitoring communication and prior to a final communication. These 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 sufficient information is available, otherwise an update will be made to the monitoring communication.

Monitoring communications

Monitoring communications are intended to:

- highlight potential safety concerns
- stimulate adverse event reporting
- instruct users to follow the manufacturer's product information/instructions for the medicine or medical device (where applicable).

These communications will advise consumers and health professionals of the nature of the potential concern, encourage consumers and health professionals to report adverse events and where appropriate emphasise that they should follow the manufacturer's product information/instructions for the medicine or medical device. As the safety concern will not have been reviewed in detail by the regulator at the time the monitoring communication is published it is unlikely that any further advice will be available.

These communications may be issued at two stages of the therapeutic product vigilance process:

- initial assessment/risk analysis step
- signal investigation/assessment step.

The criteria for issuing these communications are described below.

Initial assessment/risk analysis

Safety concerns at this stage include all those detected by the regulator. These concerns include those that are already known, coincidental events and safety signals.

Medsafe and the TGA already communicate on a regular basis to discuss new safety concerns detected by each regulator. Medsafe currently informs the TGA about concerns selected for inclusion on M[2]. Communications between the two regulators will continue and expand as part of the early warning system.

Decision criteria

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.

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. Relevant Expert Advisory Committees that may be consulted on potential safety concerns include:

In Australia - Advisory Committee on the Safety of Medical Devices (ACSMD), Advisory Committee on the Safety of Medicines (ACSOM) and Advisory Committee on the Safety of Vaccines (ACSOV).

In New Zealand- Medicines Adverse Reaction Committee (MARC), Medicines Classification Committee (MCC) and Medicines Assessment Advisory Committee (MAAC).

Signal investigation/assessment step

Safety concerns at this stage will generally only include new concerns or changes in frequency of known concerns (i.e. a safety signal).

The TGA and Medsafe regularly discuss safety concerns considered to be safety signals. Communications on these concerns will continue and expand as part of the early warning system.

Decision criteria

Safety concerns with medicines and medical devices will be considered for a monitoring communication at the Signal Investigation/Assessment 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.

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.

For medicines the definition of serious according to ICH - 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 could be significant interest in the safety concern from consumers, health professionals, government or media.

This will be determined through the volume and/or nature of enquiries received by the TGA and or Medsafe for the current issue or previous similar issues. 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. Relevant Expert Advisory Committees that may be consulted on potential safety concerns include:

In Australia – Advisory Committee on the Safety of Medical Devices (ACSMD), Advisory Committee on the Safety of Medicines (ACSOM) and Advisory Committee on the Safety of Vaccines (ACSOV).

In New Zealand- Medicines Adverse Reaction Committee (MARC), Medicines Classification Committee (MCC) and Medicines Assessment Advisory Committee (MAAC).

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. A copy of the draft communication will be shared with the other regulator. General information on these types of safety concerns and how to report will be contained on the early warning system webpages (see Attachment 1). Hypothetical examples of monitoring communications are also included in Attachment 1.

Sponsor/manufacturer engagement

The sponsor(s) of all relevant products will be informed of communications. Sponsors are requested to point out any factual inaccuracies in the communications but are not expected to provide other comments. Sponsors may also be requested to provide information about safety concerns which the regulator has decided require investigation.

Monitoring communication publication

Once the communication has been approved a copy will be provided to the other regulator and it will be published on the TGA and/or Medsafe websites. The location and format for these publications is outlined below in the section describing the webpages. It is not intended that these communications are actively provided to consumers and health professionals. However, interested parties may subscribe to a website update email list, which will notify users of these communications. Also users may subscribe to the RSS feed to receive the latest content published on the TGA Internet site.

Alert communication

The aim of the alert communication is to provide important information and recommendations about therapeutic products (including where the TGA/Medsafe has investigated a safety concern and no actions are required). Alerts will be provided once a safety concern has been investigated. At this stage the TGA/Medsafe will have concluded whether the safety concern is valid and what actions should be taken to improve the safety of the product (including if no action is required). The alert communication may be published prior to all the recommended actions being completed.

Some safety concerns may have had a monitoring communication published. Where this is the case, there will be links on the website between the alert communication and the original monitoring communication.

The TGA and Medsafe regularly discuss safety concerns including the results of any investigations undertaken. The TGA and Medsafe will share information on decisions to issue alerts.

Decision criteria

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

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

This will be according to the existing therapeutic product vigilance procedures of the TGA or Medsafe.

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.

This will be determined through 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. Relevant Expert Advisory Committees that may be consulted on potential safety concerns include:

In Australia – Advisory Committee on the Safety of Medical Devices (ACSMD), Advisory Committee on the Safety of Medicines (ACSOM) and Advisory Committee on the Safety of Vaccines (ACSOV).

In New Zealand- Medicines Adverse Reaction Committee (MARC), Medicines Classification Committee (MCC) and Medicines Assessment Advisory Committee (MAAC).

Content of alert communications

Following the decision to issue an alert, the communication will be drafted for publication on the regulator's website. A copy of the draft communication will be shared with the other regulator. General information on these types of safety concerns will be contained on the early warning system webpages (see Attachment 1). Hypothetical examples of alert communications are also included in Attachment 1.

Sponsor/manufacturer engagement

The sponsor(s) of all relevant products will be informed of communications. Sponsors are requested to point out any factual inaccuracies in the communications but are not expected to provide other comments.

Sponsors may have also been requested to provide information about the safety concern during the regulator's investigation.

Alert publication

Once the communication has been approved, a copy will be provided to the other regulator and will be published on the TGA and/or Medsafe websites. The location and format for these publications is outlined below in the section on early warning system webpages and in Attachment 1.

Alert communications will be actively shared with relevant stakeholders (including other government departments, health professionals and consumers) as well as published on the TGA and/or Medsafe websites. It is likely that for some shared concerns that the actions described in the alerts will be different. This is due to the differences in legislation, usage and healthcare systems between Australia and New Zealand.

Early Warning System Website Content

All safety communications will be published on either the TGA or Medsafe websites. Some safety concerns may be published on both websites, but in country specific format. In future, communications may also be published on the transition to ANZTPA website.

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.

Location

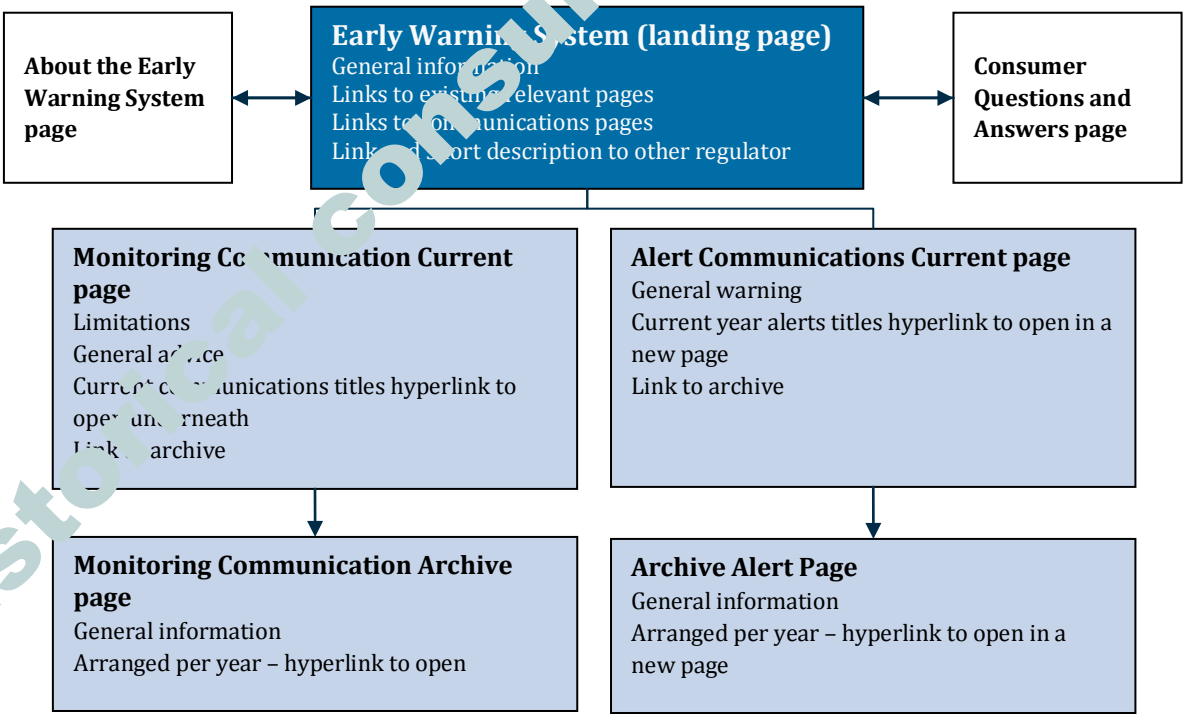
In Australia the safety communications will be located on the TGA website in the safety information tab with links from the consumers and health professional tabs. Links to the alerts will also be available in the news section.

In New Zealand the safety communications will be located on the Medsafe website under safety topics.

Structure

The structure of the early warning system website content is shown below:

Figure 2: Proposed structure of the early warning system website content



Text for Webpages

The proposed text for inclusion on the TGA website for the Early Warning System is shown in Attachment 1.

Glossary

Term	Definition
Adverse event	Any untoward medical occurrence in a patient (or care giver in the case of medical devices) who has used a therapeutic product and which does not necessarily have to have a causal relationship with this therapeutic product.
Adverse reaction	An unintended and noxious effect that is attributable to a therapeutic product used correctly.
Alert	An identified risk associated with the use of a medicine or medical device which requires urgent measures to protect patients.
ANZTPA	Australia New Zealand Therapeutic Products Agency, which will replace the TGA and Medsafe.
CARM	Centre for Adverse Reactions Monitoring. Contracted by the Ministry of Health, New Zealand to collect reports of suspected adverse reactions to medicines in New Zealand.
CMI	Consumer Medicine Information. The CMI is based on the product information/ data sheet but is written in plain language to assist consumers to use medicines safely and effectively.
Data Sheet	A summary of the known information about a product in New Zealand; known as the PI (Product Information) in Australia.
Identified Risk	An untoward occurrence for which there is adequate evidence of an association with the medicine or medical device of interest.
Medical Device	In general an instrument, apparatus, appliance, material, or other article (whether for use alone or in combination), together with any accessories or software required for its proper functioning which is intended for use in the diagnosis, prevention, monitoring, treatment or alleviation of disease; diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap; investigation, replacement or modification of the anatomy or of a physiological process; control of conception and does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but that may be assisted in its function by such means. For the legal definitions used in Australia and New Zealand, refer to the *Therapeutic Goods Act 1989* and the *Medicines Act 1981*, respectively.

Term	Definition
Medicine	A substance or preparation used in the prevention, diagnosis treatment of a disease, ailment, defect or injury or used to influence, inhibit or modify a physiological process that achieves its principal intended action by pharmacological, chemical, immunological or metabolic means. For the legal definitions used in Australia and New Zealand, refer to the *Therapeutic Goods Act 1989* and the *Medicines Act 1981*, respectively.
Medsafe	New Zealand Medicines and Medical Devices Safety Authority. Medsafe is a business unit of the Ministry of Health and the authority responsible for the regulation of therapeutic products in New Zealand.
PHARMAC	The Pharmaceutical Management Agency is the New Zealand Crown agency that decides, on behalf of District Health Boards, which medicines and related products are subsidised for the use in the community and public hospitals.
Product Information	A summary of the known information about a product, known as the PI in Australia and the data sheet in New Zealand.
PSUR/PBRER	The Periodic Safety Update Report (PSUR)/Periodic Benefit-Risk Evaluation Report (PBRER) provides 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.
Safety concern	An untoward occurrence for which there is some basis for suspicion of an association with the medicine or medical device of interest, but where this association has not been confirmed.
Safety signal	New information that suggests a new potentially causal association, or new aspect of a known association, between an intervention and an event(s) that is judged to be of sufficient likelihood to justify further action to verify.

Term	Definition
Serious (safety signal)	For medicines the definition of serious according to ICH - 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.
Sponsor	In general the company responsible for distributing a therapeutic product. For the legal definitions used in Australia and New Zealand, refer to the *Therapeutic Goods Act 1989* and the *Medicines Act 1981*, respectively.
Spontaneous report/notification	An unsolicited communication to a company, regulatory authority, or organisation that describes an adverse event in a patient given one or more therapeutic products and which does not derive from a study or organised data collection scheme.
Stimulated reporting	Reports following communication of a safety concern and describing that concern.
TGA	The Therapeutic Goods Administration is Australia's regulatory authority for therapeutic goods. The TGA carries out a range of assessment and monitoring activities to ensure therapeutic goods available in Australia are of an acceptable standard with the aim of ensuring that the Australian community has access within a reasonable time to therapeutic advances.
Therapeutic product	Any product for which therapeutic claims are made. This includes medicines, vaccines and other biological products and medical devices.

Term	Definition
Therapeutic product vigilance	The science and activities relating to the detection, assessment, understanding and prevention of adverse effects of medicines and medical devices.

Attachment 1- TGA proposed website content with examples

New web page (URL TBA)

Early Warning System

The Early Warning System includes current and historical information on safety concerns for medicines and medical devices that the TGA has identified through its therapeutic product vigilance program.

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

1. Monitoring communications

These early communications are intended to highlight potential safety concerns that are identified by the TGA. In addition, the TGA aims to stimulate further reports and research to provide more information on these safety concerns.

2. Alert communications

These communications are 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.

More information about the Early Warning System

- Early Warning System: consumer questions and answers
  Consumer questions and answers about the Early Warning System
- About the Early Warning System
  Information about the two types of communications in the Early Warning System
- Current year monitoring communications
  Links to monitoring communications issued by the TGA during the current year
- About monitoring communications
  Monitoring communications highlight potential safety concerns
- Current year alerts
  Links to alerts issued by the TGA during the current year

  About alerts
  Alerts provide important information and recommendations about therapeutic products
- Therapeutic product vigilance
  The TGA's approach to 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

New web page (URL TBA)

About the Early Warning System

The Early Warning System includes current and historical information on safety concerns for medicines and medical devices. These communications are issued as part of a joint project between the TGA and the New Zealand Medicines and Medical Devices Safety Authority (Medsafe). While the communication process is the same in both countries, the communications themselves are country-specific and the recommendations may differ because of different legislative requirements, and different availability and/or usage of certain therapeutic products between Australia and New Zealand. You can view New Zealand communications on the Medsafe website.

No therapeutic product is completely risk free. While many risks are identified before the product is used in Australia, some are identified later. The process of identifying these risks and analysing the benefit versus risk profile of a therapeutic product is described in the Therapeutic Product Vigilance section.

The known risks associated with prescription or pharmacist-only medicines are outlined in the Product Information (PI) and the Consumer Medicine Information (CMI) documents. The known risks for complementary medicines and medical devices are generally outlined in the PI/instructions for use supplied with the therapeutic product.

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

1. Monitoring communications

Early communications about potential safety concerns are provided in the monitoring communications section. The intention of these communications is to highlight potential safety concerns that are identified by the TGA. In addition, the TGA aims to stimulate further reports and research to provide more information on these safety concerns as at this stage, little information is known about the safety concern.

Not all of these concerns will result in the TGA taking an action. This may be because after investigation, the TGA has not found evidence to support a link between the events and the therapeutic product. The TGA may reinvestigate the safety concern if more information is identified at a later date.

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.

Safety concerns which identify defective medicines or medical devices supplied in the market may result in a recall action. This can include removal of the product from supply or undertaking corrective action. A summary of recent recall actions initiated in Australia can be viewed in the publicly accessible and searchable database: System for Australian Recall Actions (SARA).

Reporting adverse events to medicines and medical devices

Consumers and health professionals are encouraged to report problems with medicines, vaccines or medical devices. Your report will contribute to the TGA's monitoring of these products.

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medicine, vaccine or medical device.

Summaries of medicine adverse events already reported to the TGA can be viewed in DAEN and JAENS.

New web page (URL TBA)

Early Warning System: consumer questions and answers

- Click on the plus or minus icon next to the question to toggle the answer on or off or [Open all | Close all].
- If you want to print all questions and answers, you need to **Open all** before you print.

What are safety concerns?

A safety concern is any potential safety problem linked to a medicine or medical device. Safety concerns include known safety problems, changes to known problems, new problems and coincidental events. At the time the safety concern is detected, the TGA may not know if the concern is actually caused by the medicine or medical device.

How are safety concerns identified?

The TGA use many sources of information to identify safety concerns. These include adverse event notifications, published papers, sponsors and manufacturers' clinical studies, researchers and health professionals, and other regulatory authorities and government agencies.

What is the TGA doing about these safety concerns?

The TGA investigates safety concerns to determine if the concern is caused by a medicine or medical device. The TGA identifies all the possible information available on the safety concern and reviews this information. The TGA may also seek advice from experts, for example the Advisory Committee on the Safety of Medical Devices, and works closely with other regulatory authorities.

If there is an actual link between a therapeutic product and a safety concern, the TGA will consider the appropriate action(s) that needs to be taken to improve the safe use of the medicine or medical device.

What actions can the TGA take?

As a regulator, the TGA has to consider the balance between the benefits offered by a therapeutic product and the potential risks associated with its use for the population as a whole (or individual patient groups where the risks may be higher) before it makes a decision on an appropriate response. There are a range of actions that can follow when a potential safety problem is identified. These include:

- informing health professionals and consumers through alerts and other communications such as articles in the *Medicines Safety Update*
- requiring changes be made to the Product Information
- changing the conditions of use or narrowing the population in which it can be used
- changing the legal status of a medicine, for example making a medicine only available with a doctor's prescription
- requesting the sponsor complete a study to investigate the concern
- withdrawing or suspending the market approval for the medicine or medical device.

In some cases, no action may be recommended and the TGA will continue to monitor the safety concern.

Why is the TGA publishing these safety concerns?

The Early Warning System is designed to support better health outcomes by providing better access to information on safety concerns. It is part of the work the TGA does to monitor the safety of medicines and medical devices for consumers.

As demand for information about medicines and medical devices grows, along with Australia's ageing population, a reputable government agency publishing information on medicine and medical device safety concerns online improves public access to this important information. The TGA is committed to improving transparency to build trust and confidence in its work.

What is an adverse event?

Adverse events are unwanted and sometimes harmful outcomes from taking a medicine or using a medical device.

What is a side effect?

Side effects are known unintended effects of a medicine or medical device.

How can I find information on the known side effects of medicines and medical devices?

Information on known side effects is included in the Consumer Medicines Information (CMI), which is available for all prescription and pharmacist-only medicines in Australia. CMI provides information on the safe and effective use of a prescription or pharmacist-only medicine and is either included in the medicine pack or available in a separate leaflet from the pharmacist. You can also look up CMI information on the TGA website's CMI search facility.

The known risks for complementary medicines and medical devices are generally outlined in the product information/instructions for use supplied with the therapeutic product.

How do I report an adverse event?

If you suspect that you are experiencing an adverse event you should consult a healthcare professional. The adverse event should then be reported to the TGA using one of available reporting options outlined on the TGA website.

My medicine or medical device is mentioned in a monitoring communication, what should I do?

The TGA emphasises that patients should NOT stop using a medicine or medical device subject to a monitoring communication. If you have any concerns with a therapeutic product you are using, please contact your health professional.

The intention of these communications is to highlight potential safety concerns that are identified by the TGA and help stimulate further reports and research to provide more information on these safety concerns.

If you have experienced one of these safety concerns please submit a report to the TGA. Your report will contribute to our monitoring of these products.

My medicine or medical device is mentioned in an alert communication, what should I do?

The TGA advises all consumers to follow the advice provided in the alert communication. Consumers should NOT stop using a medicine or medical device without first seeking the advice of their health professional; unless this is advised in the alert communication.

How does the Early Warning System alert differ from the TGA Recall Communications?

The Early Warning System alert communication advises consumers, health professionals and industry about new safety information on therapeutic products following the outcome of an investigation. An alert does not necessarily mean that a product is considered to be unsafe.

A recall communication provides advice to consumers, health professionals and industry about a defective therapeutic good and the recall action undertaken in the Australian market. Recall actions are usually due to unacceptable quality, safety, efficacy /performance or presentation.

Existing web page (http://www.tga.gov.au/safety/index.htm)

Safety information

No therapeutic product is ever completely risk free. Some risks may be known when a medicine or medical device is first registered. However, some information only comes to light after more people use the products.

This section includes current and historic recalls of medicines and medical devices, advice that the TGA has issued about products, monitoring communications, information on reporting problems and how the safety of therapeutic goods is monitored.

Existing web page (http://www.tga.gov.au/safety/alerts.htm)

Alerts

Alerts provide important information and recommendations about therapeutic goods. Even though an alert has been issued, it does not necessarily mean a product has been found to be unsafe.

- Current year alerts
  Links to alerts issued by the TGA during the current year
- All alerts
  Links to alerts issued by the TGA since 1998
- About alerts
  Alerts provide important information and recommendations about therapeutic goods

Existing web page (http://www.tga.gov.au/safety/alerts-current.htm)

Current year alerts

The following alerts have been issued by the TGA in the current year.

Existing web page (http://www.tga.gov.au/safety/alerts-all.htm)

All alerts

The following alerts about therapeutic products have been issued by the TGA since 1998.

This list is also available in date order: All alerts (sorted by date)

0-9 | A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z |

Existing web page (http://www.tga.gov.au/safety/alerts-about.htm)

About alerts

The TGA issues alerts to advise consumers, health professionals and industry about new safety information regarding therapeutic products.

An alert does not necessarily mean that a product is considered to be unsafe. Alerts may explain the outcome of an investigation including any recommended actions for consumers and health professionals or a change to the availability of a product, or may advise that counterfeit or illegal products have been detected in Australia.

New web page (URL TBA)

Monitoring communications

The TGA emphasises that patients should NOT stop using a medicine or medical device subject to a monitoring communication. If you have any concerns with a therapeutic product you are using, please contact your health professional.

A monitoring communication highlights potential safety concerns identified by the TGA with a therapeutic product. The appearance of a safety concern in this section does not mean that the TGA has concluded that the medicine or medical device causes an adverse event.

All monitoring communications issued will have a subsequent communication advising of the outcome.

- Current year monitoring communications
  Links to monitoring communications issued by the TGA during the current year
- All monitoring communications
  Links to monitoring communications issued by the TGA since 2013
- About monitoring communications
  Monitoring communications highlight potential safety concerns identified by the TGA with therapeutic goods

New web page (URL TBA)

Current year monitoring communications

The TGA emphasises that patients should NOT stop using a medicine or medical device subject to a monitoring communication. If you have any concerns with a therapeutic product you are using, please contact your health professional.

The following monitoring communications have been issued by the TGA in the current year.

New web page (URL TBA)

All monitoring communications

The TGA emphasises that patients should NOT stop using a medicine or medical device subject to a monitoring communication. If you have any concerns with a therapeutic product you are using, please contact your health professional.

The following monitoring communications have been issued by the TGA since 2013.

This list is also available in date order: All monitoring communications (sorted by date)

0-9 | A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T | U | V | W | X | Y | Z |

New web page (URL TBA)

About monitoring communications

The TGA emphasises that patients should NOT stop using a medicine or medical device subject to a monitoring communication. If you have any concerns with a therapeutic product you are using, please contact your health professional.

This section contains communications issued by the TGA for safety concerns with medicines and medical devices shortly after they have been identified. These communications highlight *potential* safety concerns.

The appearance of a safety concern in this section does not mean that the TGA has concluded that the medicine or medical device causes an adverse event.

Consumers are advised to use products according to the instructions provided with the medicine or medical device. For prescription and pharmacist-only medicines, these are outlined in the Consumer Medicines Information (CMI), which is either included in the medicine pack or available in a separate leaflet from the pharmacist. You can also look up CMI information on the TGA website's CMI search facility. For complementary medicines and medical devices these are generally outlined in the product information/instructions for use supplied with the therapeutic product.

If you or someone you know has experienced one of these safety concerns please submit a report. This helps TGA to investigate these safety concerns and decide if any action needs to be taken.

It is likely that some safety concerns that resulted in monitoring communications being issued will not result in any action being taken and these communications will be updated accordingly. If the TGA's review of the safety concern concludes that there is a causal relationship with a medicine or medical device, an alert may be issued. The TGA will take appropriate action to improve the safe use of this medicine or medical device, where required.

All monitoring communications issued will have a subsequent communication advising of the outcome.

Existing web page (http://www.tga.gov.au/consumers/information-safety.htm)

Safety information for consumers

The TGA monitors the safety of therapeutic goods in Australia and can take action to address safety concerns.

The pages linked below contain information for consumers, patients and carers about the safety of medicines and medical devices.

Reporting medicine problems

- Report a problem with a medicine
  The TGA encourages health professionals and consumers to report problems with medicines (including prescription, over-the-counter and complementary medicines) and vaccines so that it can identify and respond to safety concerns.

Reporting medical device problems

- Report a problem with a medical device
  Users of medical devices are encouraged to report problems that have caused, or could cause, harm to patients, carers or others. Investigations of medical device incidents can lead to actions such as product recalls, safety alerts, product improvement, user education and compliance testing.

Product recalls

- Product recalls
  A product recall is the removal of a therapeutic good from supply on the Australian market due to an 'established deficiency in quality, efficacy or safety'.
- Safe disposal of unwanted medicines
  Unwanted medicines can be returned to local pharmacies involved in the Return Unwanted Medicines (RUM) Project

Alerts

- Alerts
  Alerts provide important information and recommendations about therapeutic products. Even though an alert has been issued, it does not necessarily mean a product has been found to be unsafe.

Monitoring communications

- Monitoring communications
  Monitoring communications aim to highlight potential safety issues with therapeutic products and to increase the available information on these potential safety issues through stimulated reporting.

Existing web page (http://www.tga.gov.au/hp/information-safety.htm)

Safety information for health professionals

Related information

- Prescribing medicines in pregnancy database

Information for health professionals about the safety of medicines and medical devices.

Recalls, alerts and monitoring communications

- Alerts
  Important safety information and recommendations about therapeutic products available in Australia
- Recalls
  Therapeutic goods removed from the market due to deficiencies in quality, efficacy or safety
- Monitoring communications
  Highlights potential safety issues with therapeutic products and encourages further reporting

Reporting problems

- Reporting problems
  Information about how to report problems with medicines and medical devices

Journals and articles

- Implanting medical devices
  The TGA has received adverse event reports that have involved incorrect devices being used or implanted into patients
- Medicines Safety Update
  Medicines Safety Update provides practical information and advice on drug safety and emerging safety issues
- Australian Adverse Drug Reactions Bulletin
  Australian Adverse Drug Reactions Bulletin from 1995 to 2009
- Medical Device Incident Reporting and Investigation Scheme (IRIS) articles
  Articles issued by the IRIS since 2001

Example 1 – Medical Device - Monitoring communication

Hearalot hearing aids

Monitoring communication

21 January 2013

The TGA has received three reports from consumers regarding their Hearalot hearing aids overheating. In each instance it was reported after replacing the battery no further heating problems were experienced.

Consumers should use the specified battery type and installation instructions in the Hearalot user manual when replacing the battery.

The TGA is continuing to monitor the rate and pattern of occurrence of this issue.

Consumers and health professionals are encouraged to report problems with medical devices. Your report will contribute to the TGA's monitoring of these products. For more information see the TGA Incident Reporting and Investigation Scheme (IRIS).

The TGA cannot give advice about an individual's medical situation. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medical device.

Example 2 – Medicine - Monitoring communication

Noxuout (morestapam)

Monitoring communication

21 January 2013

The TGA has received three reports of tendonitis suspected to have been caused by Noxuout. The three reports from healthcare professionals stated the tendonitis started one to three weeks after starting Noxuout. All the patients recovered after stopping Noxuout.

Noxuout is the trade name for morestapam. Noxuout is a new medicine used to help people with problems sleeping (insomnia). This medicine is only available in tablet form for use in adults. Like other medicines used for sleeping problems, Noxuout should only be used for short periods.

The TGA is continuing to monitor reports of adverse events associated with Noxuout.

Consumers and health professionals are encouraged to report problems with medicines. Your report will contribute to the TGA's monitoring of these products.

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medicine.

Example 3 – Medical Device - Alert communication

Speediwiz wheelchairs

Safety advisory

21 January 2013

Related information

- Recall: Speediwiz wheelchairs (Models XC-XE) 21 January 2013

Consumers, health professionals and retailers are advised that Speediwiz Manufacture Pty Ltd (SMPL), after consultation with the TGA, is recalling some models of the Speediwiz wheelchair to correct the brake mechanism.

Investigations by SMPL in conjunction with the TGA have found that the brake mechanism can fail when there is inadequate air pressure in the rear tyres. The recommended air pressure of the rear tyres is 40 – 50psi.

While no injuries have been reported, failure of the brake mechanism during use could result in serious injury.

All Speediwiz wheelchairs manufactured since July 2012 have a redesigned brake mechanism and are not affected by this issue.

The affected model numbers are:

- 10908 - Speediwiz wheelchair XC (manufactured between July 2008 – June 2012)
- 10909 - Speediwiz wheelchair XD (manufactured between July 2008 – June 2012)
- 10910 - Speediwiz wheelchair XE (manufactured between July 2008 – June 2012)

The listed Speediwiz wheelchair models can be identified from the manufacturer plate stamp which is located on the underside of the chair.

Information for consumers

If you have a Speediwiz wheelchair from one of the affected models, you can return it to the place of purchase or rental for a replacement wheelchair whilst SMPL replaces the brake mechanism.

Alternatively, you can call the SMPL toll-free customer service line on 1300 000 000 between 8:30am and 5:30pm AEDST to arrange the return of the affected product and a replacement.

If you think you may have a Speediwiz wheelchair from one of the affected models but cannot confirm the details, phone the SMPL customer service line.

Information for health professionals and retailers

If you have a Speediwiz wheelchair from one of the affected models in stock, do not sell, rent or provide them to consumers. Check all stock, including storerooms and hire pools and isolate any products from the affected models.

SMPL has written to retailers outlining the process for returning affected models and obtaining replacement stock.

Additional information

The TGA has received four reported failures of the brake mechanism not holding the Speediwiz wheelchair on a sloped surface.

The models that were found to be affected were manufactured between 2008 and 2010, with failures presenting between two and four years after manufacturer. During the investigation it was found the failures were occurring when the air pressure in the rear tyres was less than 25psi. The recommended air pressure of the rear tyres is 40 – 50psi.

Reporting problems

Consumers and health professionals are encouraged to report problems with medical devices. Your report will contribute to the TGA's monitoring of these products. For more information see the TGA Incident Reporting and Investigation Scheme (IRIS).

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medical device.

Example 4 – Medicine - Alert communication

Noxuout (morestapam) and reports of seizure

Safety advisory

1 February 2013

Related information

- Recall: Noxuout (morestapam) - Lozamed Pharmaceuticals Ltd

Patients taking Noxuout (morestapam) manufactured by Lozamed Pharmaceuticals Ltd are advised to urgently speak with their health professional to discuss alternative treatments. New clinical study information has shown that patients taking Noxuout are at risk of experiencing a seizure.

The TGA has suspended the supply of Noxuout in Australia while the safety profile of this medicine is reassessed. The sponsor Lozamed Pharmaceuticals Ltd, after consultation with the TGA is recalling all batches of Noxuout.

This alert applies only to Noxuout the trade name for morestapam. Noxuout is used to help people with sleeping problems (insomnia). This medicine is only available in tablet form for use in adults.

Information for consumers

Noxuout has been shown to cause seizures in a small number of consumers.

Seizures may include events such as black outs, confusion, deafness, out of body feeling, eyes rolling, falling down, foot stomping, hand waving, shaking, stiffening, teeth clenching or memory loss.

You should urgently speak with your health professional to discuss alternative treatments.

If you have a seizure or think you may have had a seizure you should seek medical advice straight away.

If you have any concerns arising from your use of this product, consult with your health professional.

Information for health professionals

The risk of seizure in patients taking Noxuout in the clinical study was 2.2 (adjusted OR) (95% CI 1.5-9.3) compared with no treatment.

Noxuout should not be prescribed to new patients.

Existing patients should be contacted and an alternative treatment initiated if required.

Noxuout is being recalled from all pharmacies. More information on the recall is available on the TGA website.

Additional information

A phase III double-blind randomised placebo controlled study conducted in 3,000 patients in the United States has recently been completed. The study was designed to investigate the efficacy of Noxuout in Shift-Work Sleep Disorder. Initial analysis of the study indicates an increased risk of seizure in patients taking Noxuout: adjusted OR 2.2 (95% CI 1.5-9.3). A meta-analysis of clinical study data for the insomnia indication also revealed an increased risk of seizure adjusted OR 1.8 (1.3-2.5).

In addition, four reports of seizure in patients taking Noxuout have been reported to the TGA.

Reporting problems

Consumers and health professionals are encouraged to report adverse events to medicines. Your report will contribute to the TGA's monitoring of these products.

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medicine.

Example 5 – Medicine - Alert communication

Lowklot (finagrel) - No increased risk with cancer identified

Safety advisory

14 February 2013

Health professionals and consumers are advised that there is no evidence of an increased risk of cancer associated with the blood thinning medicine Lowklot (finagrel). This advice comes following a full safety review conducted by the TGA in conjunction with the Advisory Committee on the Safety of Medicines (ACSOM). This potential risk was first highlighted by the results of an observational study published in the BMJ.

This alert applies only to Lowklot, the trade name for finagrel, manufactured by Medmiedz Ltd. Lowklot is a medicine used to thin the blood (an anticoagulant) and help prevent strokes and heart attacks. These tablets are only available on prescription from a doctor for use in adults.

Information for consumers:

No evidence of an increased risk of cancer has been found in patients taking Lowklot.

If you have any concerns or questions about this information please discuss these with your health professional.

Report any problems you experience with medicines to the TGA; see below for how to report.

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medicine.

Information for health professionals:

In Jan 2012 the BMJ published the results of an observational study showing an association between use of Lowklot and an increased risk of cancer.

The manufacturer provided the TGA with additional safety information including: results of preclinical studies, a meta-analysis of randomised controlled trials and two further observational studies conducted in the USA and United Kingdom.

There was no evidence that Lowklot had mutagenic activity in pre-clinical studies.

The meta-analysis did not find a significant increased risk of cancer: Odds Ratio 1.2 (95% CI 0.8-1.5) in patients taking Lowklot compared to placebo.

Two observational studies were conducted. A small increased risk was noted in the study comparing patients exposed to Lowklot with unexposed patients Hazard Ratio 1.32 (95% CI 1:04- 1.45). In the study comparing Lowklot with clopidogrel, no increased risk of cancer was noted Hazard Ratio 1.05 (95% CI 0.89-1.12).

The TGA and ACSOM concluded that there is no increased risk of cancer in patients taking Lowklot (finagrel).

Additional information:

In the original paper conducted using the General Practice Research Database (GPRD), an increased risk of cancer, Hazard Ratio 1.5 (95% CI 1.1-1.9), was seen in patients taking Lowklot compared to patients unexposed to Lowklot. This safety concern was further investigated by the manufacturer. A review of previously conducted studies investigating the mutagenicity and carcinogenicity of Lowklot were negative. The manufacturer conducted a meta-analysis of phase II to IV clinical studies for Lowklot. In total 17 studies including 3,587 patients exposed to Lowklot and 3,289 patients taking placebo were included in the meta-analysis. There was a slight imbalance in baseline risk factors for cancer favouring the placebo group. The risk of cancer found in the meta-analysis was an Odds Ratio 1.2 (95% CI 0.8-1.5) in patients taking Lowklot compared to placebo. ACSOM considered that this analysis did not support an increased risk of cancer. Two further observational studies were conducted. In the first study conducted using a claims database in the USA, patients exposed to Lowklot were compared to unexposed patients. A small increase in cancer risk was noted, similar to the GPRD study: Hazard Ratio 1.22 (95% CI 1:04- 1.45). It was noted during the review of this study that there was the potential for residual confounding which may have accounted for the observed association. In the second study, conducted using The Health Improvement Network (THIN) database patients taking Lowklot were compared to patients taking clopidogrel a medicine with a similar mechanism of action. This comparison was used to try to reduce bias in the study. No difference in cancer risk was noted between the two groups Hazard Ratio 1.05 (95% CI 0.89-1.12). Overall the TGA and ACSOM consider that the evidence does not support an increased risk of cancer in patients taking Lowklot.

Reporting problems

Consumers and health professionals are encouraged to report adverse events to medicines. Your report will contribute to the TGA's monitoring of these products.

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medicine.

Example 6 – Medicine - Alert communication

Germzoff (kilzamycin) - Not to be used in patients with severe renal failure

Safety advisory

Related information
- Dear Healthcare Professional letter

6 March 2013

Health professionals and consumers are advised that Germzoff (kilzamycin) should not be used in patients with severe renal failure. Information supplied by the manufacturer Kwalimed Ltd shows that exposure to Germzoff in patients with creatinine clearance less than 30ml/min was double to that in patients with normal renal function. Higher blood concentrations of Germzoff have been associated with an increased risk of serious skin reactions and liver disorders.

This alert applies only to Germzoff, the trade name for kilzamycin manufactured by Kwalimed Ltd. Germzoff is a new broad spectrum antibiotic used to treat infections such as pneumonia. This medicine is only available on prescription from a doctor in tablet injection or liquid suspension for use in adults and children.

Information for consumers

Patients with severe kidney problems should not take Germzoff. Your doctor will have informed you if you have this problem.

If you have any concerns or questions about this information please discuss these with your health professional.

Report any problems you experience with medicines to the TGA; see below for how to report.

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medicine.

Information for health professionals

A pharmacokinetic study conducted by the company showed exposure to Germzoff in patients with creatinine clearance less than 30ml/min was double that in patients with normal renal function.

Despite reducing the dose of Germzoff from 100mg daily to 25mg daily, plasma levels in patients with **severe** renal failure remained high.

Two patients with severe renal failure participating in the study experienced adverse effects: one developed an exfoliating skin reaction and the other experienced jaundice.

In patients with **moderate** renal failure a dose reduction to 50mg resulted in acceptable plasma levels.

The TGA concluded that the lack of information on safe dosing of Germzoff in patients with severe renal failure and the adverse reactions noted in the study means that Germzoff should not be used in these patients.

Additional information

Kwalimed Ltd performed a pharmacokinetic study of Germzoff in patients with mild, moderate and severe renal failure. The study was designed to test whether target plasma levels of Germzoff could be achieved with dose reductions predicted from previous pharmacokinetic studies. The results are shown in the table below.

Degree of Renal Failure	Dose of Germzoff	Mean $AUC_{(0-24)}$ (percentage difference to patients with normal renal function)	Mean C_{max} (percentage difference to patients with normal renal function)
Mild (>50-<80ml/min)	100mg	2.4µg hr/ml (25%)	312ng/ml (33%)
Moderate (30-50ml/min)	50mg	1.8µg hr/ml (-9%)	221ng/ml (-5%)
Severe (<30ml/min)	25mg	3.9µg hr/ml (102%)	421ng/ml (80%)

The predicted dose adjustment required for patients with moderate renal failure was successful. However in patients with severe renal failure the predicted dose adjustment was not successful. In addition, two patients in this group experienced serious adverse events: skin exfoliation and jaundice.

The product information is being updated to reflect this new information. In addition, the manufacturer has sent a letter to all health care professionals advising them of these changes.

Reporting problems

Consumers and health professionals are encouraged to report adverse events to medicines. Your report will contribute to the TGA's monitoring of these products.

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medicine.

Example 7 – Medical Device - Alert communication

Reliachex blood glucose test strips - Do not store in the fridge

Safety advisory

7 March 2013

Healthcare professionals and consumers are advised not to store the blood glucose test strips used in the Reliachex Blood Glucose Monitor in the fridge.

Investigations by the Medihealthchex Technologies Ltd in conjunction with the TGA into reports of unusual blood glucose readings with the Reliachex blood glucose monitoring system found no quality issues with the product and that the strips had been stored incorrectly in the fridge. Incorrect storage can lead to false or inaccurate blood glucose readings.

While no adverse outcomes were reported, unreliable blood glucose test results could result in a patient taking too much or too little insulin which poses a significant health risk.

Healthcare professionals and consumers should follow the storage conditions outlined in the instructions for use and on the labelling of the product which specify the test strips for the Reliachex Blood Glucose Monitor should be stored out of direct sunlight, in a dry place at room temperature below 30°C.

This alert applies to the blood glucose test strips that are used in the Reliachex blood glucose monitoring system made by Medihealthchex Technologies Ltd.

Information for consumers

Store Reliachex blood glucose test strips out of direct sunlight, in a dry place at room temperature below 30°C as per the manufacturer's instructions.

Reliachex blood glucose test strips that have been stored in the fridge should be discarded.

Report any problems you experience with medical devices to the TGA; see below for how to report.

Information for health professionals

Advise patients to store Reliachex blood glucose test strips out of direct sunlight, in a dry place at room temperature below 30°C as per the manufacturer's instructions.

Advise patients to discard any unused strips that have been stored incorrectly in the fridge.

Report any problems with medical devices to the TGA; see below for how to report.

Additional information

The TGA has received a total of four reports from healthcare professionals and consumers regarding this problem. The investigation by Medihealthchex Technologies Ltd and the TGA found that in each case the patient had stored the glucose test strips in the fridge, along with their insulin. The reporters noticed that the results of their glucose test were higher or lower than expected and when the reporters retested using strips not stored in the fridge; a different result was obtained. In accordance, with the manufacturer's

instructions the test strips for the Reliachex Blood Glucose Monitor should be stored out of direct sunlight, in a dry place at room temperature below 30°C.

During the investigation, a series of quality control tests were performed on retained test strip samples from the same batch numbers. All the tested strips passed and were within the expected range. There were no quality issues identified with the product.

Reporting problems

Consumers and health professionals are encouraged to report problems with medical devices. Your report will contribute to the TGA's monitoring of these products. For more information see the TGA Incident Reporting and Investigation Scheme (IRIS).

The TGA cannot give advice about an individual's medical condition. You are strongly encouraged to talk with a health professional if you are concerned about a possible adverse event associated with a medical device.

Therapeutic Goods Administration

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