



Australian Government
Department of Health
Therapeutic Goods Administration

Postmarket monitoring





Overview

- What is postmarket monitoring?
- Why is it important?
- Tools used in postmarket monitoring
- Managing risk
- Adverse events
- Risk management plans
- Signals
- Recall actions
- Pharmacovigilance Inspection Program
- Other education modules

What is postmarket monitoring?

The aim is to continually monitor and evaluate the safety and, in some cases, the efficacy or performance of therapeutic goods that are available on the market and to manage any risks associated with individual products.



Why is this important?

Not all risks can be identified before registration

Vioxx was first approved in Australia in 1999 for symptomatic treatment of osteoarthritis and rheumatoid arthritis.



Compared with placebo, this equated to one extra cardiovascular event for each 65 patients who took Vioxx for at least 18 months.



Postmarket study showed an increased risk of cardiovascular events beginning after 18 months of treatment in patients taking the recommended daily dose.

This was one catalyst for more vigorous postmarket monitoring for regulators around the world.

Vioxx was withdrawn from the market worldwide in 2004.



Tools used in postmarket monitoring



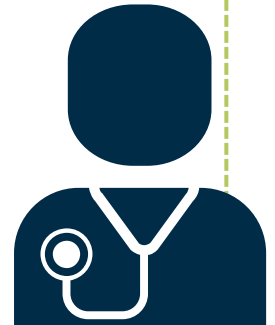
Risk management
plans (RMPs)



Adverse event
reporting
and
Pharmacovigilance
Inspection Program
(PVIP)



Environmental
scanning (seeking
confidential advice
from other regulators
and review of medical
literature, regulatory
news, media and
other sources)



As a future health professional, you can help by [learning how to report adverse events](#)



Managing risk

- The TGA works on a risk-benefit assessment of products at a population level. The benefit of taking the medicine or using the device should be greater than the possible adverse events.
- Higher levels of risk may be acceptable for a product used to treat a terminal illness, but not for a common or minor complaint.



Definition of an adverse event

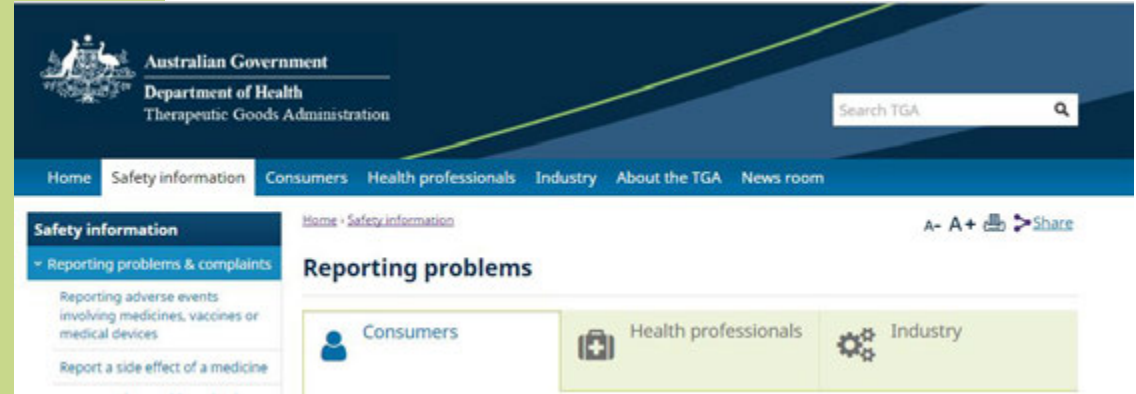
For both medicines and medical devices: an event that resulted in, or could have resulted in, serious injury, illness or death.

A medical device adverse event can also be associated with the use (or misuse) of a medical device. This may include difficulties or malfunctions, such as problems with getting the device to operate, the need for repeated repairs, difficulty of use or difficulty with cleaning after use.



Your role as a health professional

- You play an important role in monitoring the safety of therapeutic goods by reporting any suspected adverse events to the TGA.
- Reports can be made online, or by phone, fax or email.
- Visit the TGA website for more information about reporting.



www.tga.gov.au



What should you report?

The TGA is particularly interested in:

- serious or unexpected reactions to medicines
(this is explained further on the next slide)

serious medicine interactions

defects or problems with medical devices that have resulted, or could have resulted, in adverse events.



Reporting serious and unexpected reactions to medicines



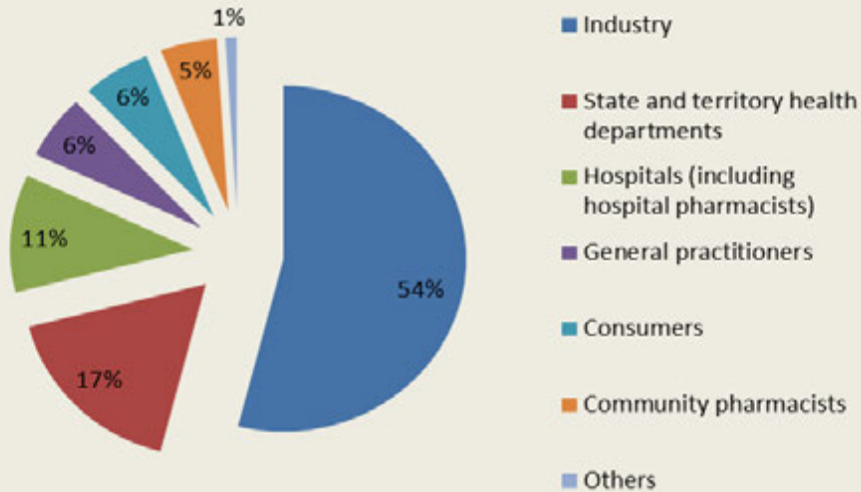
It is most important to report serious and unexpected reactions to medicines. These are distinct from well known side effects. For example, we would not expect reports of:

- tiredness after taking an opiate based painkiller
- nausea or diarrhoea after taking certain antibiotics.

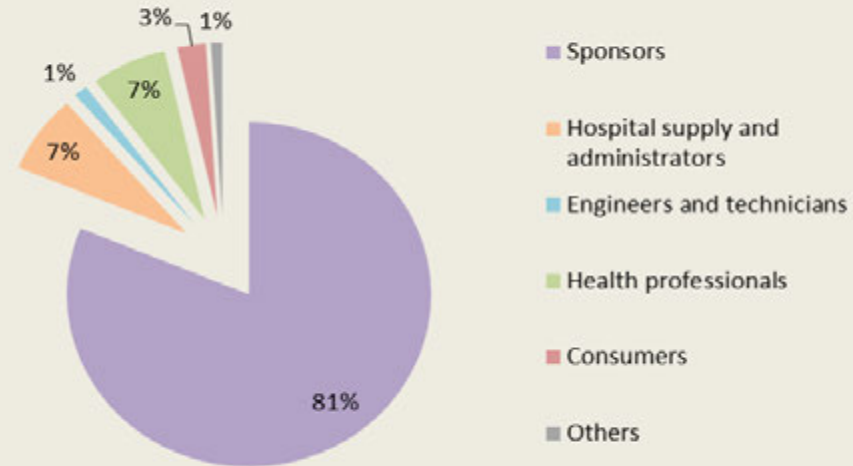
Who currently reports adverse events?

2016 data

Medicines



Medical Devices



Why Risk Management Plans? (RMPs)

Real-world use of a medicine or biological identifies issues that may not have been discovered during a clinical trial

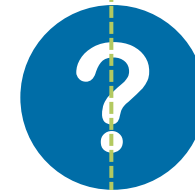
RMPs are completed by sponsors as part of the registration process for high-risk medicines and biologicals (made from or contains human cells or human tissue)

They outline the risk management system for a product once it is available for use in Australia

RMPs are living documents that cover the lifecycle of a product and inform the periodic safety update reports



Key elements of an RMP



Safety specification

Safety profile of a medicine or biological, including known and potential safety concerns



Pharmacovigilance activities

Plan for how safety concerns will be monitored and how further information will be collected



Risk minimisation activities

Plan for how the risks associated with the use of the product will be minimised



Safety signals

How we respond

- Signals are information collected from one or more sources that show a potentially causal relationship between a product and an adverse event.
- There are three steps in the signal investigation process.



Step 1 – detecting signals

Involves a review of adverse event reports, international monitoring activities and reports, published literature and post-approval studies to identify harmful effects



Step 2 – assessing signals

Involves determining the:

- nature
- magnitude
- health significance

of potential safety problems and their impact on the overall risk-benefit of the product.

This process takes into consideration factors such as whether it is a serious adverse event in a few patients or a moderate adverse event in a large number of patients.



Step 3 – responding to signals

Regulatory actions taken to mitigate risk include:

- communication of information for consumers, health professionals and industry regarding the problem
- alteration of the product label
- recall of goods from sale or use, or for correction
- changes to the conditions of registration
- suspension or cancellation of the product.

TGAUPDATE

Alerts & recalls

28 July 2017

[Gadolinium-based contrast agents for MRI scans](#)

Safety advisory - potential retention in the brain but no known adverse effects

27 July 2017

[Infections associated with heater-cooler devices](#)

Update

Case study – one report can make a difference

Report that an epidural catheter, which is normally clear, was yellow when removed from the packaging for use.

Upon testing, the yellow catheter was found to be cytotoxic. New, clear catheters (of the same brand) were also found to be cytotoxic.

Further analysis found a plasticiser used to soften the catheter, n-butyl benzene sulfonamide, is a neurotoxin. The manufacturer had been using it for 30 years with no reports of related adverse events.

The catheter was reformulated worldwide due to the TGA's discovery.

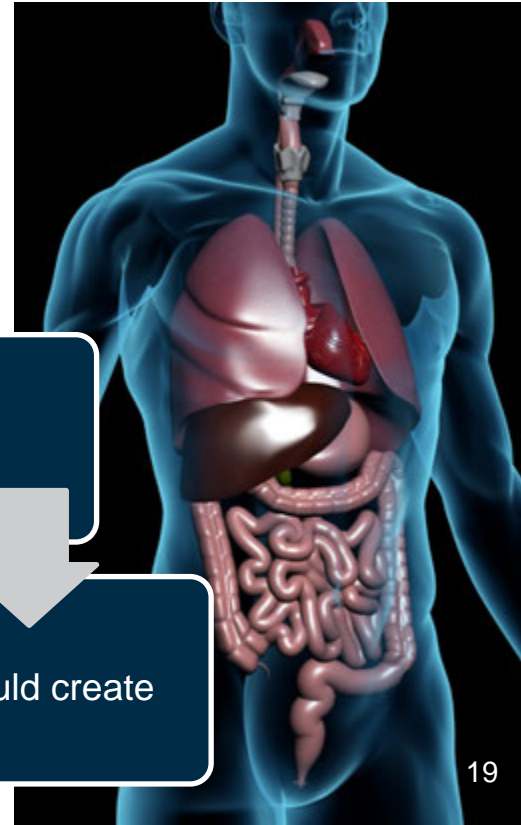


Case study – a handful of reports can uncover previously unknown safety issues

The TGA received eight reports of serious liver injury associated with the use of lumiracoxib (an anti-inflammatory used to treat osteoarthritis) including two fatalities, two liver transplants, severe jaundice and acute hepatitis without liver failure.

The TGA investigated the reports and received expert advice that the apparent rate of severe liver injury with lumiracoxib appeared greater than for other similar medicines.

The TGA immediately cancelled the registration of all forms of lumiracoxib in Australia, on the grounds that failure to do so would create an imminent risk of death, serious illness or serious injury.





Recall actions

A recall action is taken to resolve a problem with a therapeutic good already supplied in the market. There are three distinct types of recall actions:

- **Recall:** The permanent removal of an affected therapeutic good from supply or use in the market.
- **Recall for product correction:** Repair, modification, adjustment or re-labelling of a therapeutic good.
- **Hazard alert:** Information issued to health professionals about issues or deficiencies relating to an implanted medical device or biological product.

Search databases

Australian Register of
Therapeutic Goods (ARTG)

Adverse events (DAEN)

Recalls (SARA)

Prescribing medicines in
pregnancy

Consumer Medicines
Information (CMI)

Product Information (PI)

Medicine shortages

Australian Public Assessment
Reports for prescription
medicines (AusPARs)

Ingredients

You can search for recall
actions via this link at
www.tga.gov.au



Pharmacovigilance Inspection Program

The TGA's Pharmacovigilance Inspection Program (PVIP) has been introduced to help sponsors meet pharmacovigilance obligations by:

- educating sponsors on their pharmacovigilance requirements
- verifying Australian sponsors' compliance with existing requirements
- working with sponsors to ensure systems are collecting current information on the safety and efficacy of their medicines.

For more details visit:

[www.tga.gov.au/
pharmacovigilance-
inspection-program](http://www.tga.gov.au/pharmacovigilance-inspection-program)



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- Consultations
- Publications
- Scheduling



Other education modules include:

Introduction to the TGA

Medicines

Biologicals

Devices

Good manufacturing practice