Australian Government
Department of Health
Therapeutic Goods Administration

Medicines and vaccines adverse event reports

Statistics for 2013

Version 1.0, June 2014

TGA Health Safety Regulation

About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health, and is responsible for regulating medicines and medical devices.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy (performance), when necessary.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to consumers outweigh any risks associated with the use of medicines and medical devices.
- The TGA relies on the public, healthcare professionals and industry to report problems with medicines or medical devices. TGA investigates reports received by it to determine any necessary regulatory action.
- To report a problem with a medicine or medical device, please see the information on the TGA website <http://www.tga.gov.au>.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Office of Product Review	5/06/2014

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Foreword

The Therapeutic Goods Administration (TGA) is responsible for regulating medicines, vaccines and biologicals, including monitoring the ongoing safety, quality and efficacy of these products once they have been included on the Australian Register of Therapeutic Goods (ARTG), the TGA continues to monitor it through product vigilance activities.

On an annual basis, the TGA's Office of Product Review (OPR) of the TGA prepares a report for incorporation into the Department of Health publication *Australian Statistics on Medicines*. *Australian Statistics on Medicines* is produced by the Drug Utilisation Sub-Committee (DUSC) of the Pharmaceutical Benefits Advisory Committee (PBAC) and is aimed at providing comprehensive and valid statistics on the Australian use of medicines and vaccines in the public domain to allow access by all interested parties.

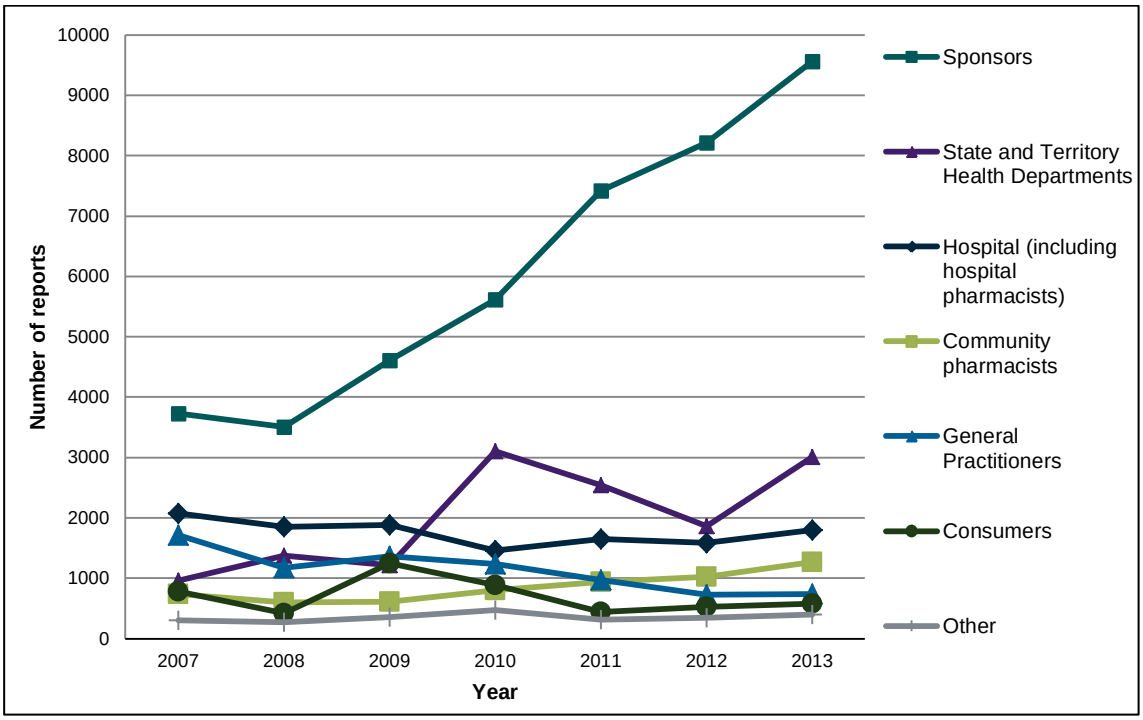
This report from the OPR includes a brief overview on the following aspects of post-market monitoring of medicines and vaccines in Australia:

- Adverse event reporting statistics for 2013
- Processing and use of adverse event reports
- Reporting adverse events
- Expert advisory committees
- Medicines Safety Update
- Product vigilance

Adverse event reporting statistics for 2013

The TGA's reporting system for adverse events began in the late 1960s with the computerised database dating back to the early 1970s. By the end of 2013 there were approximately 278,000 reports of suspected adverse events in the database.

Figure 1: Origin of medicine and vaccine adverse events reported to the TGA (2007-13)



In 2013 the TGA received approximately 17,500 reports of adverse events. As shown in Figure 1, the majority of reports made in 2013 were by sponsors. The number of reports made by sponsors has steadily increased over the past five years, more than doubling since 2009. Approximately 55% (9563) of adverse event reports received by the TGA in 2013 were from sponsors, 10% (1794) from hospitals and hospital pharmacists, 4% (733) from general practitioners (GPs), 17% (3011) from State and Territory Health Departments (Adverse Events Following Immunisation), 7% (1268) from community pharmacists and 3% (574) from consumers.

In each group, the number of reports received increased in 2013 from the 2012 levels, with State and Territory Health Departments registering the biggest proportional increase (up over 60% from 1857 reports in 2012 to 3011 reports in 2013). However, this increase followed two years of decline in 2011 and 2012.

While health professionals are encouraged to report suspected adverse events directly to the TGA although they can also report directly to the sponsor or manufacturer.

Processing and use of adverse event reports

The OPR assessed adverse event reports submitted to the TGA by checking for the presence of 'minimum' details, i.e. an individual patient, an adverse event, at least one (suspected) drug, and preferably an identifiable reporting health professional. The specific reaction terms are identified along with the suspected, interacting or 'other' drugs and these are entered into the database.

The OPR assesses causality of adverse event(s) and in some cases requests further clinical or laboratory information from the reporter. Medical officers review serious reports and OPR staff regularly analyse reporting data to identify potential safety signals.

Reports are forwarded to the Uppsala Monitoring Centre in Sweden, which administers the World Health Organization Collaborating Centre for International Drug Monitoring. This global

database began in 1968 as a pilot program involving 10 nations, including Australia, and now receives reports from more than 80 nations.

Database of Adverse Event Notifications

Information in the publicly searchable Database of Adverse Event Notifications (DAEN) comes from reports made to the TGA by a wide range of sources, including members of the public, general practitioners, nurses, other health professionals and the therapeutic goods industry. Reports in this database start from 1 January 1971 up to three months prior to the date of access. The TGA uses this three-month period to investigate each adverse event report.

The DAEN, which was launched in 2012, was created to support better health outcomes by providing access to the information that the TGA gathers while monitoring medicine and vaccine safety in Australia.

Reporting adverse events

The TGA encourages the reporting of all suspected adverse events to medicines and vaccines available in Australia, including prescription medicines, over the counter and complementary medicines. The reporting of seemingly insignificant or common adverse events can contribute to the TGA's investigation of a potential safety signal.

Sponsors of all medicines and vaccines on the ARTG have mandatory reporting requirements regarding adverse events.

The TGA particularly requests reports of:

- suspected adverse events involving new medicines and vaccines
- suspected drug interactions
- unexplained adverse events (i.e. reactions that are not described in the Product Information)
- serious adverse events, such as those suspected of causing:
  - inability to work
  - admission to hospital
  - prolongation of hospitalisation
  - increased investigation or treatment costs
  - danger to life
  - birth defects
  - death.

For further information about reporting suspected adverse events, visit the TGA website (click on 'Report a Problem').

Expert advisory committees

Advisory Committee on the Safety of Medicines

The Advisory Committee on the Safety of Medicines (ACSOM) was established in January 2010 to provide expert advice to the TGA about safety issues under investigation and the appropriateness of Risk Management Plans (RMPs). RMPs outline sponsors' plans to monitor and communicate risks, and are evaluated as part of the registration process for new medicines. RMPs accompany applications for registration of high risk medicines, such as new chemical entities. RMPs characterise and pro-actively manage risks relating to a medicine over its entire life cycle. ACSOM also provides advice to the TGA on other matters related to pharmacovigilance, including the detection, assessment, understanding and prevention of adverse events.

Advisory Committee on the Safety of Vaccines

The government's Review of the management of adverse effects associated with Panvax and Fluvax (the Horvath Review), amongst other things, included a recommendation to establish a working party to review governance of the vaccine safety system. Following a recommendation from the Horvath Review in 2012 'to consider the current governance arrangements for monitoring and responding to vaccine safety issues in Australia and make recommendations for an improved system of governance for vaccine safety monitoring' the Advisory Committee on the Safety of Vaccines (ACSOV) was established in the Therapeutic Goods Regulations. The functions of ACSOV are to provide advice and make recommendations to the Minister for Health, the TGA and the Office of Health Protection on the safety, risk assessment and risk management of vaccines.

Medicines Safety Update

The *Medicines Safety Update* is published six times a year in *Australian Prescriber*, and also on the TGA website. The *Medicines Safety Update* replaced the *Australian Adverse Drug Reactions Bulletin* in 2010.

The following articles were published in *Medicines Safety Update* during 2013:

- Progressive multifocal leukoencephalopathy - a rare but serious disease
- Thyroxine (Eutroxsig and Oroxine) and fractures
- Oral bowel cleansing products - serious electrolyte disturbances
- Montelukast - neuropsychiatric risks
- Use of 2013 seasonal influenza vaccines in children
- Denosumab and severe hypocalcaemia
- Anticholinergics and cognitive impairment
- System for Australian Recall Actions
- Changes to cough and cold medicines for use in children
- Update - Progressive multifocal leukoencephalopathy (PML)
- Mitigating risks of dabigatran: right patient, right dose and careful clinical monitoring

- New dabigatran contraindication
- Vancomycin and nephrotoxicity
- Dapagliflozin - new chemical entity
- Dexmedetomidine hydrochloride and cardiovascular events
- Bevacizumab and necrotising fasciitis
- Atomoxetine and suicidality in children and adolescents
- Rotavirus vaccination and the risk of intussusception
- Drug-induced liver injury
- Pioglitazone risk-benefit review
- 5-alpha reductase inhibitors and risk of high-grade prostate cancer
- Duloxetine and serotonin syndrome
- Minocycline and intracranial hypertension

Product vigilance

The TGA applies a risk management approach to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety and efficacy. Once a therapeutic product is approved, the TGA continues to monitor the product in the market through therapeutic product vigilance activities.

The aim of therapeutic product vigilance is to continually monitor and evaluate the safety and efficacy (performance) profile of therapeutic goods and to manage any risks associated with individual products over their life cycle. The TGA's therapeutic product vigilance framework is available on the TGA website at Therapeutic product vigilance.

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

Sponsors have the primary responsibility for the safety of any therapeutic products they import into, supply in or export from Australia. Sponsors must comply with legislative requirements for therapeutic product vigilance under the *Therapeutic Goods Act 1989* (the Act) and there are applicable offences and penalties under the Act for not complying. The legislative requirements for therapeutic product vigilance vary depending on the type of therapeutic good.

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

The TGA defines therapeutic product vigilance tools as tools designed to facilitate the collection and evaluation of information pertaining to the benefits and risks associated with the use of therapeutic products. The main product vigilance tools used by the OPR are adverse event reports, RMPs and Periodic Safety Update Reports (PSURs).

Adverse event reports are reports of any untoward occurrence in a patient administered a medicine and which does not necessarily have a causal relationship with the medicine. An

adverse event can therefore be any unfavourable and unintended sign, symptom, or disease temporally associated with the use of a medicine, whether or not considered related to this medicine.

RMPs provide a summary of the known important safety information about the therapeutic product, plans to identify and characterise known or potential safety concerns and plans to minimise any identified or potential safety risk. A full outline of the scope of RMPs is above (see 'Expert advisory committee'). PSURs give an annual overview of the safety of the drug, including adverse events, a summary of the registration status of the drug world-wide, actions taken for safety reasons, the world-wide usage of the drug and an analysis of safety requirements. Sponsors must submit PSURs for at least three years after registration of a drug.

An important aspect of product vigilance is ensuring there are mechanisms to communicate safety information to both consumers and health professionals. To achieve this, the TGA publishes Australian Public Assessment Reports (AusPARs) about recently registered prescription medicines on the TGA website. AusPARs outline the findings of the TGA's evaluation of a product including important effectiveness and safety information. The TGA also publishes the Product Information (PI) and Consumer Medicine Information (CMI) for prescription and some non-prescription medicines, as well as safety alerts, Early Warning System monitoring communications and *Medicines Safety Update*, which provide information and recommendations about therapeutic good

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