Australian Government

Department of Health

Therapeutic Goods Administration

Product regulation according to risk

Overview of the way the Therapeutic Goods Administration (TGA) considers risks and benefits during the evaluation and post-market monitoring of products

Our ‘risk-based’ approach to regulating therapeutic goods is designed to ensure that regulation is only used where absolutely needed and, then, only to the extent needed to protect and advance public health. In practice, this means the level of regulation—and our regulation and compliance efforts—is commensurate with the risks posed by particular therapeutic goods.

Evaluation of products

We regulate therapeutic goods by examining evidence of their risks and comparing that to the evidence associated with their benefits. The identified level of risk determines:

- the amount and type of information we need to review
- the degree of scrutiny necessary before the product can be made available in Australia and the level of safety monitoring once it is available.

The amount of regulatory oversight needed to appropriately manage risks depends on the nature and intended use of the product, and the level of risk ultimately determines the manner in which the public can gain access to that product. For example, many lower risk products such as herbal and multi-vitamin products may be safely sold in supermarkets, whereas higher risk medicines such as blood pressure medications may only be supplied with a prescription from a suitably qualified health professional. The risk-based approach to regulation allows greater effort to be directed to those therapeutic goods which pose greater risks to a patient's health.

Medicines

All medicines carry a risk of producing adverse reactions in some patients. Products carrying a higher risk, including all prescription medicines and over-the-counter medicines such as painkillers and allergy tablets, receive a higher degree of pre-market assessment and, where the benefits of taking the medicine outweigh the risk of adverse reactions, are registered on the Australian Register of Therapeutic Goods (ARTG). An example might be the approval of a new cancer medicine for a target population where it is known the medicine is likely to result in relatively severe side effects.

Registered medicines

We conduct detailed evaluations of higher risk (registered) medicines before they can be approved for use in Australia in order to fully evaluate the balance between the benefits and the risk. The data submitted in support of a new registered medicine should establish the quality, safety and effectiveness of the proposed product for the proposed usage (indication). Data fall into three main categories; quality control, safety and clinical use. Those applications that include active ingredients with a long history of safe use, such as paracetamol, are not required to be assessed to the same level as a new prescription antibiotic. After evaluation of data, the TGA delegate, usually a senior medical officer, considers the overall application and either grants approval to include the product on the ARTG for specified use, or rejects the application. These decisions are open to appeal by the applicant or other interested party affected by the decision.

Listed medicines

Products such as vitamins, minerals, sunscreens and herbal complementary medicines carry a lower risk, and receive a lesser degree of initial assessment, than higher risk medicines. These products are listed on the ARTG provided certain conditions are met. The listing process for complementary medicines is based on an applicant certifying that the claims made about the effectiveness of their product are accurate, that the relevant quality and labelling and packaging standards have been followed, that the medicine contains only approved ingredients and that the manufacturing facilities and processes have been assessed for compliance with standards of Good Manufacturing Practice.

Unlike registered medicines, we don't individually evaluate lower risk 'listed' medicines before they can be available for use in Australia. However, they cannot claim to treat serious diseases and can be removed from the market if the claims made for the products are inappropriate or any of those certifications are not correct.

Medical devices

Medical devices differ from medicines as they generally have a physical or mechanical effect on the body, or are used to measure (or monitor) the body and its functions.

The way in which we assess medical devices (including the type of information required) is different than that used for medicines, but the risk-based approach is the same. The higher the potential risks of a medical device, the more they need to be examined and monitored. Lower risk devices (such as bandages) rely on the applicant's certification of compliance with regulatory requirements (in a similar way to complementary medicines), whereas higher risk devices (such as pacemakers) involve a direct evaluation of the available evidence by our officers.

Medical devices are assigned into one of five main classifications depending on the level of risk they pose:

Classification(s)	Risk level	Examples
Class I	Low	• Crutches • Hospital beds
Class I - supplied sterile Class I - with a measuring function Class IIa	Low to Medium	• Sterile surgical gloves • Clinical thermometer measuring body temperature • Dental drills or ultrasound machines
Class IIb	Medium to High	• Surgical lasers • Diagnostic X-ray
Class III	High	• Prosthetic heart valves • Absorbable surgical sutures
Active implantable medical devices (AIMD)	High	• Pacemakers • Artificial heart

In vitro diagnostic devices

In vitro diagnostic medical devices (IVDs) are typically pathology tests (and related instrumentation) used to carry out testing on human samples where the results are intended to assist in clinical diagnosis or in making decisions concerning clinical management. Classification of IVDs considers the health risk (either of the public or an individual) that may occur where an incorrect result arises from their use. The higher the potential risk an incorrect result would pose, the higher the classification:

Classification	Risk level/ Description	Examples
Class 1 IVD	no public health risk or low personal risk	• Microscope counting chambers • Prepared (ready to use) microbiological culture media
Class 2 IVD	low public health risk or moderate personal risk	• Pregnancy and fertility self testing kits • Urine self testing kits
Class 3 IVD	moderate public health risk or high personal risk	• Tests to detect the presence of (or exposure to) a sexually transmitted agent
Class 4 IVD	high public health risk	• All tests used by the Australian Red Cross Blood Service for testing of the blood supply

Biologicals

Biologicals are a distinct group of therapeutic goods which are made from, or contain, human cells or human tissue. The regulation of biologicals also uses a risk-based approach, and utilises a comprehensive system of assessment and controls that must be completed before products can be marketed in Australia.

The nature of biologicals means that they can pose risks that do not arise with other therapeutic goods, such as the risk of infectious disease transmission, or other unforeseen biological reactions. Unlike a medicine which can be immediately discontinued if serious adverse events occur, it is often not feasible to discontinue therapy with a biological, if for example the therapy has involved implantation of living cells into a patient.

The range of raw materials and manufacturing processes used to produce biologicals can lead to very different levels of risk to a patient. Regulation of biologicals utilises four classifications based on risk.

Class	Description	Risk level	Examples
1	Risks associated with use should be very low, and satisfactorily managed by a high level of oversight, e.g. manufactured under expert medical supervision	Very low	<none identified to date>
2	Product undergoes minimal manipulation when manufactured, therefore retains the original properties/functions of the original donor material The final product is used for the same purpose/function as the original donor material	Low	• Frozen bone • Human heart valves • Corneas
3	Product undergoes manufacturing processes above and beyond those defined as 'minimal manipulation' The manufacturing process has not altered the original properties/ functions of the original donor material The final product can be used for the same basic function, or a different purpose, as the original donor material	Medium	• Demineralised bone • Chondrocytes for cartilage repair
4	Product undergoes manufacturing processes above and beyond those defined as 'minimal manipulation' The manufacturing process has altered an original property/function of the original donor material The final product can be used for the same basic function, or a different purpose, as the original donor material	High	• Genetically modified cells

Unapproved products

Generally, any product which claims to have, or has, a therapeutic use must be authorised by us for that purpose by being listed, registered or included in the ARTG before it can be supplied in Australia. However, there are some exemptions from this requirement. Examples include products that are considered to be very low risk, for example:

- certain shampoos for the treatment or prevention of dandruff
- certain homoeopathic preparations
- household and commercial grade disinfectants without specific efficacy claims.

Access to unapproved products

In recognition that there are circumstances where patients need access to therapeutic goods that are not on the ARTG, we manage several programs to enable this. These programs include the Special Access Scheme, Authorised Prescribers scheme, and clinical trial schemes. It is also possible for individuals to import unapproved products for personal use. In these situations, most of the risk – benefit consideration is undertaken by a health professional working with an individual patient.

Post-market monitoring

Once a therapeutic product is approved, we continue to monitor the product on the market. The aim of such therapeutic product vigilance is to continually monitor and evaluate the safety and efficacy (performance) profile of the medicine, device or biological and to manage any risks associated with individual products.

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

Tool	Description	Applied to products such as	Primary Source of Information
Risk management plan (RMP)	Summary of the known important safety information about the therapeutic product (safety specifications) Plans to identify and characterise known or potential safety concerns (pharmacovigilance plan) and to minimise any identified or potential safety risk (risk minimisation plan) Higher risk medicines may require an assessment of benefit	Registered medicines	• sponsors
Adverse event (AE) reporting	Reports regarding deficiencies in labelling, instructions or packaging, defective components, performance failures, poor construction or design of medical devices marketed in Australia Reports on harmful and unintended responses to biologicals marketed in Australia	Medical devices Biologicals	• sponsors • health professionals • patients and consumers
Adverse reaction (AR) reporting	Reports on harmful and unintended responses to drugs in clinical trials or marketed in Australia Expedited reporting of serious unexpected clinical trials adverse drug reactions occurring inside or outside Australia	Listed medicines Registered medicines	• sponsors • health professionals • patients and consumers • clinical trial sponsors
Annual reports for medical devices	A periodic comprehensive assessment of the world wide complaint data of a medical device	Medical devices classified as AIMD, Class III and implantable Class IIb	• sponsors
Pharmacovigilance audits	Inspection of a manufacturer's records of adverse drug reactions and reporting of unusual failure in safety and efficacy of new drugs to the TGA A medical device manufacturer's adverse event records are inspected as part of the Quality Management System (QMS) assessment	Listed medicines Registered medicines Biologicals Medical Devices	• manufacturers
Environmental scanning	Collection and review of scientific and medical literature, media reports and regulatory news to identify safety issues that require further investigation	Listed medicines Registered medicines Medical devices Biologicals	• media • academia • governments • industry • consumers

A risk-based process has been developed for the screening and prioritisation of investigations. However, all identified issues with products are recorded and acted on within a time frame appropriate to their impact on public health. For example, if death or serious injury is potentially attributed to a medicine or device, these reports are acted on with the highest urgency.

There may be different requirements for a new product where there is limited information from 'real world' usage with patients. Therapeutic product vigilance evaluation involves the ongoing assessment of the benefits and risks of a product (including data from adverse event reports, adverse reaction reports, clinical trials, 'meta-analysis' of sets of reports or of studies reported in the medical literature, observational studies, etc.) and the assurance that benefits outweigh the risks for a given population during clinical trials and following its market authorisation by us.

We use both qualitative and quantitative methodologies when performing benefit-risk assessment reviews and also engage collaboratively with international stakeholders such as the Council for International Organizations of Medical Sciences and other regulators to refine these methodologies.

We often seek advice from the Advisory Committee on the Safety of Medicines (ACSOM) on the safety of medicines and risk assessment and risk management of medicines, and from the Advisory Committee on the Safety of Medical Devices (ACSMD) on the safety, risk assessment, risk management and performance of medical devices.

Reporting on vigilance activities

We report on the monitoring and evaluation of information related to the safety and efficacy of marketed therapeutic products through a variety of means. Information is shared with the public and with health professionals through the Medicine Safety Updates (MSU) included in Australian Prescriber and through safety alerts published on our website. We have also established mechanisms to alert the public to recalls of therapeutic products, to provide the public with adverse event data associated with medicines and medical devices and to provide the public with an early warning communication system to advise of potential safety issues for medicines and medical devices.

We share vigilance data with state and territory health departments and other partners, such as the National Centre for Immunisation Research and Surveillance, and also provide adverse event information to the World Health Organization and overseas regulatory agencies.

Outcomes of vigilance activities

We have a range of options available to rectify issues that may arise from monitoring of products in the market. These options range in severity from placing additional conditions on supply of products, requiring variations to be made to product information documents, through to suspension or cancellation of the product from the ARTG. The *Therapeutic Goods Act 1989* (the Act) also provides for a range of civil and criminal sanctions to be sought where breaches of the Act or therapeutic goods regulations can be demonstrated. In using our powers, we apply a measured approach and deal with compliance issues in a manner proportionate to the risk posed to public health.