Australian Government
Department of Health
Therapeutic Goods Administration

The Therapeutic Goods Administration's risk management approach to the regulation of therapeutic goods

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TGA Health Safety Regulation

Contents

About this guidance

This guidance outlines the broad approach adopted by the Therapeutic Goods Administration (TGA) to identify and manage risk associated with therapeutic goods.

Role of the TGA

We regulate and monitor therapeutic goods through:

- pre-market assessment
- post-market monitoring and enforcement of standards
- licensing of Australian manufacturers and verifying overseas manufacturers' compliance with the same standards as their Australian counterparts
- compliance and enforcement activities to address alleged breaches of the regulatory requirements.

We also play a role in the Australian Government's implementation of the National Medicines Policy.

For more information refer to:

- TGA regulatory framework
- Product regulation according to risk
- About the work of the TGA – a risk management approach

Medicines

Australia has a two-tiered system for the regulation of medicines:

- Higher risk medicines must be registered in the Australian Register of Therapeutic Goods (ARTG), which involves individually evaluating the quality, safety and efficacy (effectiveness) of the product.
- Lower risk medicines containing pre-approved, low-risk ingredients and that make limited claims can be listed in the ARTG.

The different types of medicines that must be registered or listed are set out in the *Therapeutic Goods Regulations 1990*.

Regardless of whether a medicine is registered or listed in the ARTG, it must be manufactured in a licensed or approved facility in accordance with the principles of good manufacturing practice (GMP).

For more information refer to:

- Medicines and TGA classifications
- Medicines

Risk management options

Having identified and evaluated the risks associated with a new medicine we consider options to determine the most appropriate means to manage potential risks.

The legislative framework provides the risk management options available to us. These options include:

- **Refusal of entry in the** ARTG where the risks of a medicine outweigh the benefits.
- **Application of conditions on registration** for products intended for supply in Australia.
- **Application of conditions relating to the manufacture** of products, such as allowing only certain manufacturers to manufacture a product.
- **Requirement of the sponsor to adhere to an agreed** Risk Management Plan for products intended for supply in Australia.
- **Requirement of the sponsor to meet all** pharmacovigilance **reporting responsibilities** for listed or registered medicines supplied to the Australian market.
- Scheduling **decisions** to control how medicines are made available to the public.
- **Labelling requirements** where we stipulate particular information that must be included in the packaging or on the label of a medicine, this might include a health warning.
- **Specific conditions on supply** such as restricting supply and use of the medicine to hospitals only.
- **Require information to be included in** the Product Information (PI) and Consumer Medicines Information (CMI) leaflet for a given product.

Manufacturing medicines

We apply risk management practices to risks posed through the manufacture of a medicine. We do this through licensing, inspections and good manufacturing (GMP) compliance assessments of manufacturers.

Our focus is on ensuring that manufacturers build quality into their manufacturing processes to minimise risk. For medicines, we do this by requiring manufacturers to comply with the Code of Good Manufacturing Practice (GMP).

> GMP is used internationally to describe a set of principles and procedures which, when followed by manufacturers of therapeutic goods, helps ensure that each batch of a therapeutic good is safe, reliable and of consistent high quality.

Licensing of Australian manufacturers

With certain exceptions, Australian manufacturers of medicines are required to hold a manufacturing licence.

Before licensing a manufacturer, we assess the manufacturer's compliance with the relevant code of good manufacturing principles (GMP) through an on-site inspection. We undertake a detailed risk assessment of the manufacturer's facilities, equipment, practices and processes. This enables us to determine the appropriate action (or treatment option). Actions we can take include:

- **Refusing to issue a manufacturing licence** until the manufacturer has demonstrated that they have comprehensively designed and correctly implemented systems of quality assurance that incorporate GMP principles and which build a high level of quality control into each batch of their product.
- **Issuing of a manufacturing licence subject to conditions**, for example, conditions may be applied so that the manufacturer may only undertake certain steps in the manufacturing process or may only manufacture certain products.

For more information refer to Manufacturing medicines.

Assessment of overseas manufacturers

Overseas manufacturers of therapeutic goods supplied to Australia are required to meet an acceptable standard of good manufacturing practice (GMP) comparable to that required by Australian manufacturers.

Australian sponsors of products manufactured overseas must also obtain TGA approval for overseas manufacturers wishing to supply therapeutic goods to the Australian market.

While our GMP inspectors will conduct on-site inspections of the overseas manufacturers where required, we have entered into various international arrangements with other countries and regulatory authorities that allow us to use inspections conducted by these regulatory authorities as part of the GMP clearance process in lieu of performing our own on-site inspections.

Blood and haematopoietic progenitor cells (HPCs)

Blood, blood components and haematopoietic progenitor cells (HPCs) are regulated as medicines under the *Therapeutic Goods Act 1989*. However, they are **not** required to be entered into the Australian Register of Therapeutic Goods (ARTG).

Plasma derivatives are regulated as prescription medicines subject to full regulation under provisions requiring standards, licensing of manufacture and inclusion in the ARTG after review of manufacturing, pre-clinical and clinical data.

Some blood, blood components and haematopoietic progenitor cells are exempt from TGA oversight to allow for autologous and directed donations under the supervision of a medical practitioner.

Manufacturing blood and haematopoietic progenitor cells (HPCs)

The potential risks relating to blood, blood components and HPCs are managed through good manufacturing (GMP) inspections and licensing of manufacturers. These processes include the evaluation the Technical Master File (TMF) against relevant standards. The technical and scientific information in a TMF is expected to demonstrate the safety and quality of the product.

The risk assessment and risk management processes for ensuring compliance with good manufacturing practice (GMP) requirements are essentially the same as those described for the

manufacture of medicines and the same options to refuse to issue a licence or to issue a licence subject to conditions apply.

Biologicals

Biologicals are a distinct group of therapeutic products.

For more information refer to:

- Biologicals
- Australian regulatory guidelines for biologicals
- Classification of biologicals

Once we have reviewed of all risks associated with the different aspects of a biological product, a senior officer of the TGA will review the reports and determine what action is appropriate. The advice of independent expert advisory committees may also be sought on key issues such as for new products or major extensions of clinical indications.

Manufacturing biologicals

We also evaluate and manage risks that may be posed through the manufacture of biologicals. The requirements are equivalent to those discussed for manufacturing medicines, except that the requirements for a biological are contained within the Australian code of good manufacturing practice for human blood and blood components, tissues and human cellular therapy.

Medical devices and IVDs

The regulation of medical devices and IVDs incorporates accepted best practice relating to safety, quality and risk management procedures and adopts the principles of the International Medical Device Regulators Forum (IMDRF).

Medical devices including *in vitro* diagnostic medical devices (IVD) are assessed against the Essential Principles and in line with their intended purpose and risk-based classification.

For more information refer to:

- Overview of medical devices and IVD regulation
- Medical devices

Monitoring and review

We share responsibility for post-market risk management with sponsors, manufacturers, healthcare providers and consumers.

Each participant has a role in monitoring and evaluating adverse events associated with therapeutic goods as well as taking appropriate corrective action.

For more information refer to Post market monitoring.

Monitoring and review of medicines

Our post-market monitoring activities enable us to identify and evaluate any risks associated with the formulation, manufacture, labelling, safety monitoring and advertising of medicines once they have entered the market-place.

Under the *Therapeutic Goods Act 1989*, sponsors of medicines on the Australian Register of Therapeutic Goods (ARTG) also have mandatory pharmacovigilance responsibilities.

Some of the ways we monitor compliance include:

- monitoring of adverse events reports and recalls
- sample testing by the Laboratories Branch
- review of safety-related information submitted by sponsors or published in scientific literature
- random and targeted desk-top reviews of selected listed products
- full safety and efficacy reviews of products and substances
- review and response to intelligence and tip-offs.

We also work to ensure that Australian and international manufacturers operate in a way that results in their products meeting required standards. We conduct regular inspections of manufacturers, both in Australia and overseas, to ensure they continue to meet these standards. Where inspections or other GMP compliance signals identify that manufacturing standards are not being met, we may take compliance actions including suspending or revoking manufacturing licences of Australian manufacturers or conditioning or cancelling GMP Clearances for overseas manufacturers.

As a result of this monitoring, information might be identified that leads to a re-evaluation of the risks posed by a particular therapeutic product.

Monitoring and review of medical devices

Once a medical device has been approved for supply in Australia we undertake post-market monitoring to ensure that products continue to meet all the regulatory, safety, and performance requirements and standards that were required for the approval.

For more information refer to Post-market reviews.

The Australian Regulatory Guidelines for Medical Devices (ARGMD) provides detailed information for sponsors and manufacturers about their post-market responsibilities including:

- procedures to collect information from users
- procedures for reporting incidents and performance issues
- evidence that appropriate conformity assessment procedures have been applied
- reporting of adverse events (including threshold criteria for adverse events reporting)
- reporting exemption rules.

Compliance

Our post-market compliance activities relate to the monitoring of the continuing safety, quality and efficacy of therapeutic goods once they are on the market.

We use a combination of monitoring strategies to support our compliance programs. Our monitoring programs are both proactive and responsive and include acting upon signals and reports of non-compliance from a number of external sources.

For more information refer to Compliance management.

Communication and consultation

All participants in the development and delivery of therapeutic goods have a role to play in maintaining a benefit-risk balance by making sure that products are developed, tested, manufactured, labelled, prescribed, dispensed and used in a way that maximises benefit and minimises risk, when used as intended.

Communication and consultation are important at each step of the risk management process. We actively consult with our stakeholders to promote understanding and improve the efficiency and effectiveness of the regulatory framework.

Effective internal and external communication ensures that those responsible for implementing risk management, and those with a vested interest, understand the basis on which decisions are made and why particular actions are required.

For more information refer to the Stakeholder engagement framework.

Internal stakeholders

The effective management of both product and compliance risks depends on the collection, collation and analysis of information from all regulatory areas of the TGA.

Communication and collaboration between our different regulatory areas are facilitated by TGA being structured along functional responsibilities. This allows us to identify existing interdependencies to maximise our ability to identify and manage product safety risks and regulated entity compliance risks. This is supplemented by collaboration within the Regulatory Compliance and Risk Committee (RCRC).

Applying a whole-of-regulatory-cycle view of therapeutic goods and regulated entities allows us to identify risks and tailor appropriate risk management strategies.

External stakeholders

Communication with stakeholders is also critical for effective risk management:

- we provide guidance and information that is up to date, clear, accessible and concise through media appropriate to the target audience
- we consider the impact on the regulated entities and engage with industry groups and representatives of affected stakeholders, including consumer representatives where appropriate, before changing our policies, processes and service standards
- we establish cooperative and collaborative relationships with stakeholders to improve the efficiency and effectiveness of the regulatory framework.

Key external stakeholders

Communication and consultation with external stakeholders ensures that there is a continuous feedback loop and that information from a wide variety of sources is available to assist us in our role in risk assessment and management of therapeutic goods.

Our key external stakeholders are:

- consumers
- healthcare practitioners
- industry (sponsors and manufacturers of therapeutic goods)
- other government agencies including state and territory governments
- international regulatory bodies.

Communication and consultation mechanisms

We have a number of measures in place to ensure our stakeholders are kept informed about developments within the TGA, are well educated about the regulatory requirements and are provided the opportunity to provide feedback. These measure include, but are not limited to:

- the TGA website which is a primary source of information for consumers, healthcare practitioners and industry
- use of social media to share links and information about safety alerts, recalls, current issues and events
- a variety of email lists to which stakeholders can subscribe to receive updates
- public consultations
- industry, healthcare professionals, state and territory government health departments and consumer representation on a number of TGA committees
- regular meetings with industry, health practitioner and consumer representatives through our involvement in a variety of conferences, forums and other events
- collaboration with state and territory governments. For example, each state and territory has a State Recall Co-ordinator that assists us with the recall of products
- we survey our stakeholders each year to help evaluate our performance
- we work collaboratively with several international agencies and regulators.

For more information refer to About consultations.

Version history

Version	Description of change	Author	Effective date
V1.0	Original	Deloitte	20/07/2004
V2.0	Update to reflect regulatory changes	Office of Regulatory Integrity	06/05/2011
V3.0	Update to include Biologicals Regulatory Framework	Office of Regulatory Integrity	01/09/2011
V4.0	Update to Risk Management Standards	Office of Regulatory Integrity	09/09/2011
V5.0	Rewrite and update	Regulatory Guidance	23/02/2021

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