Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

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

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TABLE OF CONTENTS

GLOSSARY OF TERMS AND ACRONYMS USED

ARTG	Australian Register of Therapeutic Goods
Risk	The chance of something happening that will have an impact upon objectives. It is measured in terms of consequence and likelihood (AS/NZS 4360:1999)
Risk analysis	A systematic use of available information to determine how often specified events may occur and the magnitude of their consequences
Risk assessment	The overall process of risk analysis and risk evaluation
Risk evaluation	The process used to determine risk management priorities by comparing the level of risk against predetermined standards, target risk levels or other criteria
Risk management	The culture, process and structures that are directed towards the effective management of potential opportunities and adverse effects
TGA	Therapeutic Goods Administration
TG Act	*Therapeutic Goods Act 1989*

CHAPTER 1: INTRODUCTION

The Australian community has an expectation that therapeutic goods are safe and of high quality, to a standard equal to that in comparable countries. The objective of the *Therapeutic Goods Act 1989* (the TG Act) is to provide a national framework for the regulation of therapeutic goods in Australia, so as to ensure their quality, safety, efficacy and timely availability.

The Therapeutic Goods Administration (TGA), as part of the Australian Government Department of Health and Ageing, has responsibility for administering the TG Act. Essentially, any product, unless exempt, for which therapeutic claims are made must be included in the Australian Register of Therapeutic Goods (ARTG) before it can be supplied in Australia.

The TGA adopts a risk management approach to regulating therapeutic goods.

In essence, this means that the TGA:

- identifies, assesses and evaluates the risks posed by therapeutic goods;
- applies any measures necessary for treating the risks posed; and
- monitors and reviews the risks over time.

The purpose of this document is to describe the broad risk management approach adopted by the TGA. It is intended that this document will be updated as the regulatory systems changes through future legislative amendments.

CHAPTER 2: BACKGROUND INFORMATION ABOUT RISK ASSESSMENT AND RISK MANAGEMENT

Part A: What is risk management?

Risk management is "the systematic application of management policies, procedures and practices to the tasks of identifying, analysing, assessing, treating and monitoring risks".[1]

Risk is thought of as being a measure of the combination of the likelihood and the consequence of an undesirable event. A precursor to any management of risk (reduction of likelihood or consequence or both) is to:

- identify and clarify the events that are considered undesirable;
- qualify or quantify the likelihood and consequence of these events (the risk); and
- evaluate each risk and decide if they are acceptable or require some action.

In other words risk management is about defining what can go wrong, why and what can be done[2]. Risk management doesn't mean that risks can be prevented or avoided completely. Nor is risk management about risk without appropriate management strategies. Risk management is really about reducing the impact of risk to an acceptable level[3].

In the context of the TGA's regulation of therapeutic goods, a risk management approach is used by the TGA to identify, analyse, assess, treat and monitor risks associated with therapeutic goods.

Part B: What is risk assessment?

To manage risks and prevent undesired outcomes, risks first must be identified, analysed and assessed. Risk assessment means determining the likelihood of a risk being realised, what can cause this and what effect is likely.

Following assessment, decisions can be made as to whether the risks are sufficiently important to require management. If the regulator decides to

[1] Standards Association of Australia – AS/NZ 4360:1999 Risk Management.
[2] Risk Management in the Department of Health and Family Services, April 1998.
[3] Ibid.

manage a particular risk, an appropriate method of treatment must be chosen, applied and regularly reviewed.[4]

Continued monitoring and review are necessary for successful risk management because risks not only change over time but their relative significance may also change, as may the mechanisms and tools to manage the risks[5].

Part C: The risk management process

The risk management process generally involves 7 steps:

1. Establishing the context. For example, defining the relationship between the organisation and its environment, understanding the organisation's capabilities and identifying the internal and external stakeholders of the organisation.

2. Risk Identification. This involves identifying the risks that need to be managed.

3. Risk Analysis. The objectives of analysis are to separate out the minor acceptable risks from the major risks and to provide data to assist in the evaluation and treatment of risks. Risk analysis involves consideration of the sources of risk, their consequences and the likelihood that those consequences may occur.

4. Risk Evaluation. Risk evaluation involves comparing the level of risk found during the analysis process with previously established risk criteria.

5. Risk Treatment. This involves identifying the range of options for treating risk, assessing those options, preparing risk treatment plans and implementing them.

6. Monitoring and Review. It is necessary to monitor risks, the effectiveness of the risk treatment plan, strategies and the management system which is set up to control implementation. Risks and the effectiveness of control measures need to be monitored to ensure changing circumstances do not alter priorities.

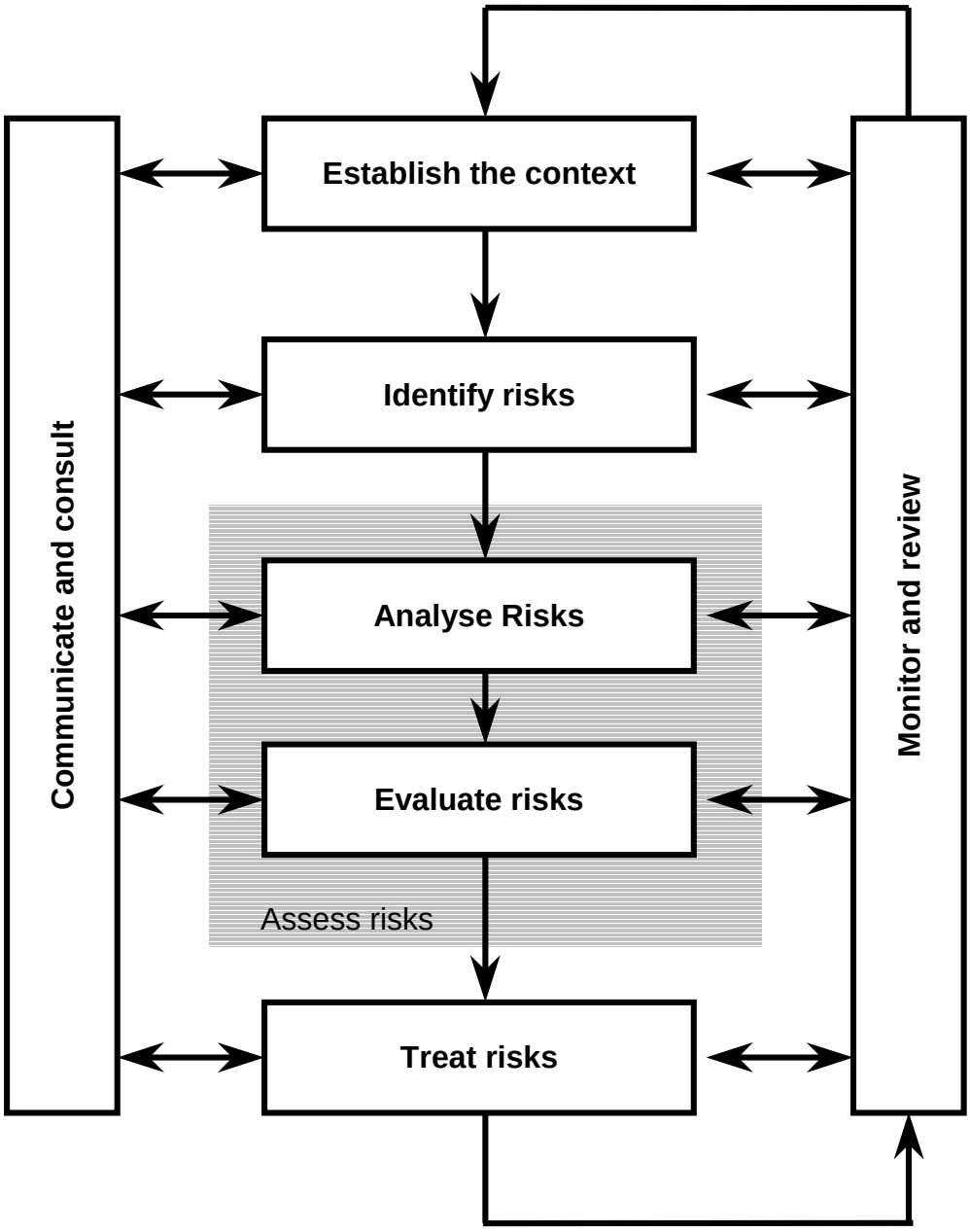
7. Communication and Consultation. This is an integral part of all aspects of the risk management process.

[4] Australian National Audit Office, Audit Report No. 12 1995-96 – Risk Management by Commonwealth Consumer Product Safety Regulators.
[5] Ibid.

The process detailed above is one that is applied by various areas of the TGA to various aspects of their work in assessing and managing the risks posed by therapeutic goods. The purpose of this document is to summarise how this risk management process is applied by the TGA.

Following is a diagram taken from the Standards Australia publication "A basic introduction to managing risk" that describes, very simply, the risk management process.

Figure 1: Risk Management overview (AS/NZS 4360:1999)



CHAPTER 3: ESTABLISHING THE CONTEXT FOR RISK ASSESSMENT BY THE TGA

Part A: Background/Context

As noted in the previous Chapter, the first part of the risk management process is establishing the context.

Establishing the context within which the TGA operates is critical to ensuring that the TGA develops and applies comprehensive and effective risk management strategies.

Establishing the context means:

- examining the relationship between the TGA and its environment and in particular the crucial elements which might support or impair the TGA's ability to manage risks;
- understanding the organisation and its capabilities as well as its goals and objectives and the strategies in place to achieve them; and
- identifying the internal and external stakeholders of the TGA and their perceptions of the organisation and its role.

Part B: The relationship between the TGA and its environment

The TGA operates in an environment where there are clear expectations about the quality, safety, efficacy and availability of therapeutic goods supplied in Australia. There are a range of potential risks associated with the supply and use of therapeutic goods that may impact on these expectations.

For example, there are many different sources of risk associated with therapeutic goods, including that:

- the product itself may pose risks– ingredients in the product, dosage form of the product, strength of a product, side effects, toxicity, potential harm through prolonged use;
- the way that the product is manufactured may pose risks – poor manufacturing processes can mean that the product does not contain the ingredients that it should, contains contaminants etc;

- the way the product is prescribed by a medical practitioner may present risk – for example if a doctor has insufficient information about the product or the patient or if the doctor misinterprets the patient's symptoms or the circumstances under which the product should or shouldn't be prescribed; and

- the way the product is used by the patient may pose risks – for example, if information for use is not sufficient (labelling), if the patient does not sufficiently understand how to use the product or if the patient inappropriately self-diagnoses and mistreats.

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.

Risk assessment and management occurs at each of these levels and by all participants in the system:

- sponsors of therapeutic goods, identify and evaluate risks (including through animal studies and clinical trials and *in vitro* work) before approaching the TGA for clearance to market products;

- manufacturers of therapeutic goods build quality assurance mechanisms into the manufacturing processes and test every batch of product to ensure that it meets the quality standards determined by the TGA – these manufacturing processes are subject to TGA approval and audit;

- the TGA evaluates the risks of individual therapeutic goods and the ingredients used in them, for the population they are intended for;

- the healthcare provider (the medical practitioner) evaluates risks for the individual patient; and

- the consumer evaluates risks in terms of their personal values, based on information provided about the product.

Crucial to understanding the risk assessment and management approach adopted by the TGA is understanding this broader context in which the TGA operates.

Part C: The TGA's role

The TGA plays a role in the management of risks associated with therapeutic goods by:

- identifying, analysing and evaluating the risks posed by a product before it can be approved for supply in Australia (pre-market product assessment or evaluation);

- identifying, analysing and evaluating the risks posed by manufacturing processes before a manufacturer is issued with a licence to manufacture therapeutic goods (licensing of manufacturers); and

- identifying, analysing and evaluating any risks that may arise following approval of the product and licensing of the manufacturer (post market surveillance).

This broad risk management framework is established in the therapeutic goods legislation which sets out the TGA's legislated responsibilities.

Each of the different areas within the agency are responsible for different aspects of the overall risk management strategy. These areas develop risk management strategies (consistent with the overall risk management approach described in the legislation) to guide their work (these strategies are described in subsequent chapters).

The TGA as a whole relies on effective and timely communication within the agency to ensure appropriate risk identification, analysis, evaluation and treatment. Further information about communication within the TGA is included in Chapter 7 of this document.

Part D: The TGA's internal and external stakeholders

The TGA has a wide range of internal and external stakeholders, including:

- consumers;
- industry (sponsors and manufacturers of therapeutic goods);
- the staff of the TGA;
- the Minister;
- the Parliament;
- health service providers;
- government agencies; and
- international organisations.

Knowing the stakeholders of the organisation, assists the TGA to assess the consequences of risk in the latter stages of risk analysis.

Communication with stakeholders is also critical for effective risk management. For example:

- the TGA needs to be able to effectively communicate with the community at large in the event of adverse drug reactions and recall of products. The community also provides valuable input to the TGA about new policies and practices;

- the TGA needs to be in regular contact with healthcare practitioners to, among other things, encourage them to report any adverse events associated with therapeutic goods;

- the TGA needs to provide guidance and assistance to industry to help them comply with the legislation. Consistent with good regulatory practice, the TGA believes that effective communication with industry is the key to ensuring compliance. Ongoing feedback from industry is an important part of the risk management approach applied by the TGA;

- State and Territory governments have a direct interest and involvement in the TGA's administration of the national regulatory scheme; and

- the TGA has agreements with a number of other regulatory bodies to enable the TGA to recognise manufacturers who have relevant certifications from overseas regulatory bodies with an equivalent regulatory system. In order for this approach to operate effectively, close communication between the TGA and the other international regulators is critical.

Further detail about the TGA's approach to communication and consultation with stakeholders is included in Chapter 7 of this document.

CHAPTER 4: IDENTIFYING, ANALYSING, EVALUATING AND TREATING THE RISKS POSED BY THERAPEUTIC GOODS

Part A: Background/Context

As detailed in Chapter 3 of this document there are many different sources of risk associated with therapeutic goods.

For example:

- the product itself may pose risks– ingredients in the product, dosage form of the product, strength of a product, side effects, toxicity, potential harm through prolonged use; and

- the way that the product is manufactured may pose risks – poor manufacturing processes can mean that the product does not contain the ingredients that it should, contains contaminants, etc.

The sponsor of the therapeutic good is ultimately responsible for ensuring that the product is safe and effective for use by consumers.

However, the TGA applies a system of oversight for identifying, analysing and evaluating the risks associated with the product itself, and the manufacturing process, to provide consumers with additional confidence in the overall system.

The approach adopted by the TGA differs slightly in relation to the regulation of medicines and medical devices. In both cases the TGA adopts a risk management approach, however the mechanisms used to identify and manage risks are different (consistent with the different processes and requirements set out in the therapeutic goods legislation).

Following is a description of the risk assessment and management approach adopted by the TGA in relation to medicines, medical devices, blood and tissues. This Chapter also includes a summary of the TGA's approach to the licensing of manufacturer's of therapeutic goods.

Part B: Medicines

Section I: Background

Before a medicine can be supplied in Australia[6] it must be listed or registered on the Australian Register of Therapeutic Goods (ARTG).

Whether a medicine is listed or registered depends on the level of risk posed by the medicine.

The TGA uses the following main risk evaluation criteria to determine whether a certain type of medicine must be registered or listed:

- the ingredients, including whether the medicine contains a substance scheduled in the Standard for the Uniform Scheduling of Drugs and Poisons;
- the dosage and dosage form of the product;
- the promotional or therapeutic claims made for the product;
- whether the medicines use can result in significant side effects;
- whether the medicine is used to treat life-threatening or very serious illness; and
- whether there are any adverse effects from prolonged use or inappropriate self-medication.

These general criteria determine whether a certain type of medicine should be "registered" or "listed" on the ARTG. The different classes of product that must be registered or listed are set out in the Therapeutic Goods Regulations.

Having classified the product as registered or listed (based on risk) this then determines the level of evaluation undertaken (further risk assessment).

All products that are classified as "registrable" must undergo a detailed pre-market risk assessment and evaluation by the TGA.

The TGA systematically applies management policies, procedures and practices to the tasks of identifying, analysing, assessing and treating the risks posed by such medicines before they are may be supplied to consumers.

[6] Subject to any exemptions detailed in the legislation.

Section II: Registered medicines

The identification, analysis and evaluation of risks associated with registrable medicines involves a number of steps.

- Different experts within and outside the TGA undertake a risk assessment of different sources of risk (chemistry, quality control and laboratory aspects, pharmacological and toxicological aspects, and clinical data). All of these areas use a range of tools to assist them to identify and analyse the risks posed by the medicines.

- Evaluation reports are prepared independently by evaluators for each area. Each evaluation report is a comprehensive critical analysis of the data submitted, including data relating to the known pharmacological profile of the product and its ingredients, the extent and quality of supporting data and the validity of any conclusions drawn from the data.

- The evaluation reports are intended to fully describe what is known about the risks and benefits based on the data. In developing evaluation reports, evaluators are encouraged to routinely seek additional information from the sponsoring company on specific issues of concern as they arise.

- When the evaluation reports are prepared they are reviewed by a senior officer of the TGA before acceptance. They are then provided to the sponsoring company for comment. Companies may choose, in certain circumstances, to submit supplementary data to address concerns raised. They may also more routinely correspond directly with the senior officer of the TGA to resolve any outstanding matters or issues of concern.

    - In relation to the quality of medicines, specifications are agreed with companies for products to be supplied to Australia. The specifications reduce risk to the Australian public by ensuring that medicines where used as intended and stored as directed are likely to remain potent throughout their shelf life and are unlikely to contain impurities or other substances which may be a threat to consumers or to health workers.

- When the evaluations on all of the risks associated with the different aspects of the product have been completed a senior officer of the TGA will review the reports and determine what action is appropriate. The advice of independent expert advisory committees may be sought on key issues such as for new products or major extensions of indications.

Having identified, analysed and evaluated the risks, the TGA determines the appropriate treatment options.

As the TGA operates within a legislative framework the options available to the TGA for the treatment of risk are detailed in the TG Act and Regulations.

The treatment options available to the TGA include the following:

- refusal of entry on the ARTG. This treatment option avoids the risk entirely by not allowing the supply of the therapeutic good that generates the risk. If the TGA considers (on the basis of its evaluation of the risks and benefits posed by a medicine) that the likelihood of the risks being realised is great and the consequences are significant, then the TGA can refuse entry on the ARTG meaning that the medicine cannot be supplied to consumers;

- application of conditions on registration. The TGA can stipulate that the product may only be supplied in Australia subject to certain conditions being met. The purpose of conditions would be to minimise (treat) any risks;

- application of conditions relating to manufacture of the goods. The TGA can apply conditions to the manufacture of the product. For example, only certain manufacturers may be permitted to manufacture the product;

- providing advice regarding scheduling. The TGA or an expert advisory committee may choose to advise the National Drugs and Poison Schedule Committee of concerns about the drug and recommend it consider restrictions on access to particular medical groups. In this way, supply of a particular high risk medicine is further restricted as a part of the risk treatment process;

- labelling. The TGA may prescribe certain information that must be included in the packaging of the medicine or on the label of the medicine;

- specific conditions on supply. The TGA can, for example, restrict supply use of the medicine to hospitals only; and

- where required, information to be included in the Product Information (PI) and Consumer Medicines Information (CMI) leaflet. Again the TGA may prescribe certain information that must be included in the PI and the CMI for a given product – in the case of the PI, this is subject to TGA approval.

In the context of having identified and analysed the risks, the TGA evaluates the treatment options and the most appropriate means to manage any risks posed.

This forms part of the overall evaluation of the medicine.

Section III: Listed medicines

Medicines that are listed on the ARTG are not subject to pre-market evaluation. This is because on the basis of a risk assessment the TGA has determined that the products are low risk. The products are low risk because, in general:

- they may only contain ingredients approved for use in listed medicines, usually well known, established ingredients, with a long history of use, such as vitamin and mineral products;
- the ingredients have well established quality and safety profiles;
- the products have commonly used manufacturing techniques;
- the products may only be used for indications consistent with low risk;
- they do not contain substances that are scheduled in the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP) or otherwise restricted (eg included in Part 4 of the Schedule 4 of the Therapeutic Goods Regulations).

For example, most complementary medicines (eg. herbal, vitamin and mineral products) are listed medicines.

If after analysing the risks, the TGA is satisfied that an ingredient is low risk and suitable for use in a listed medicine, then the ingredient (or type or class of ingredient) is prescribed as such in the Therapeutic Goods Regulations.

A sponsor may then "self-assess" their medicine as being listable (subject to the medicine meeting all the legislated criteria for listing).

The medicine is entered on the ARTG following self-assessment by the sponsor and electronic checking by the TGA's Electronic Listing Facility (ELF) software to ensure that the product is actually eligible for listing.

In order to be eligible for listing, the manufacturer of the medicine must comply with the Code of Good Manufacturing Practice and be licensed by the TGA as having an appropriate standard of GMP compliance. This provides a level of assurance of the quality of the medicine.

- GMP compliance is also required for manufacturers of registered medicines – further information regarding the requirements for licensing of manufacturers is included in Part D of this Chapter.

The sponsor must also certify that they hold evidence of efficacy and that the medicine is safe for its intended purpose. The TG Act provides the TGA with

the power to require (for the purpose of review) information relating to the quality, safety and efficacy of listed medicines.

Essential to any risk management approach is the ability to monitor and review risk assessments and treatment options. This enables the TGA to "test" on an ongoing basis the appropriateness of the classifications (listable and registrable) and the treatment options applied. Further information is included in Chapter 5 about how the TGA undertakes monitoring and review of classifications of therapeutic goods.

Part C: Manufacturing medicines

Section I: Background/Context

Described above, is the process employed by the TGA to identify, analyse, evaluate and treat the inherent risks associated with a medicine.

The TGA also applies risk management practices to manage risks that may be posed through the manufacture of a medicine.

For example, poor manufacturing processes may lead to contamination of a medicine, incorrect quantities of active ingredients in the medicine, or reduced shelf life of the medicine.

The focus of the TGA is on ensuring that manufacturers build quality into their manufacturing processes to minimise the likelihood and consequence of events occurring that produce a level of risk.

In the case of medicines, the TGA does this by requiring manufacturers to comply with the Code of Good Manufacturing Practice (GMP) (the system for devices is slightly different and is described below).

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.

The TGA identifies, analyses and evaluates manufacturing risk through licensing and auditing of manufacturers of medicines.

Section II: Licensing of manufacturers

Australian manufacturers

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

To obtain a licence to manufacture medicines, a manufacturer must demonstrate compliance with manufacturing principles including GMP.

Before licensing a manufacturer, the TGA assesses the manufacturer's compliance with the relevant Code of GMP through an on-site audit.

This enables the TGA to undertake a detailed risk assessment of the manufacturer's facilities, equipment, practices and processes and enables the TGA to determine the appropriate action (or treatment option). The treatment options may 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 good manufacturing principles and which build a high level of quality control into each batch of their product; and

- issuing 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.

Overseas manufacturers

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

Australian sponsors of products manufactured overseas must obtain TGA approval for overseas manufacturers wishing to supply therapeutic goods to the Australian market. This can be achieved by one of two means.

GMP clearance of overseas manufacturers

An application form must be completed for each manufacturing site, attaching the relevant GMP evidence (evidence of the standard of manufacture). The application and attached evidence is assessed by the TGA to ensure that the goods are manufactured to a standard of GMP equivalent to that expected of Australian manufacturers of the same goods.

If acceptable documentary GMP evidence cannot be provided, the sponsor may request the TGA to liaise with the relevant overseas regulatory agency or conformity assessment body to confirm the status of the manufacturer.

The TGA will only accept GMP certification from countries that have acceptable standards of GMP. These are:

- countries with whom Australia has entered into Mutual Recognition Agreements (MRA Countries) – Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Liechtenstein, Luxembourg, Netherlands, New Zealand, Norway, Portugal, Singapore, Spain, Sweden and United Kingdom;

- members of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) – all MRA countries (above) except Luxembourg and New Zealand, as well as Canada, Czech Republic, Hungary, Malaysia, Romania, Slovak Republic and Switzerland; and

- other countries with whom the TGA has additional arrangements – Japan and the United States.

On-site audits of overseas manufacturers

If GMP evidence can not be obtained or is unavailable, the sponsor must submit an application form requesting an on-site audit of the overseas manufacturer, in the same manner as that conducted for the Australian manufacturers (by TGA GMP auditors).

Section III: Auditing of manufacturers

Scheduling of audits

All licensed manufacturers are subject to ongoing audit by the TGA to check ongoing compliance with the relevant manufacturing principles.

The TGA schedules audits based on risk. The risk profile for a particular manufacturer is developed taking into account a number of factors including:

- type of products manufactured;

- results of previous GMP audit;

- significant changes within the company (for example, changes to key personnel, building, equipment or products);

- adverse drug reaction reports, medicine problem reports and medical device incident reports;

- results of testing by TGA Laboratories arising from random or targeted sampling of products;

- any recalls of products not meeting safety and/or quality standards;

- adverse comments from other agencies/bodies;

- post-licensing surveillance investigations; and

- intelligence tip offs.

From information obtained from these sources the TGA determines the period between audits (eg the audit schedule and the relative priority accorded to the audit of different manufacturers) and the most appropriate means for undertaking the audit (for example, announced or unannounced audit).

Consistent with good risk management practices, the TGA constantly monitors and reviews audit schedules. There is a continual re-assessment of the prioritisation of a given quarter's audits based on new applications received, new information received and the need to undertake unscheduled audits (based on the often rapidly changing status of many of the factors listed above).

Conduct of audits

Audits undertaken by the TGA are generally on-site audits. This means that expert auditors from the TGA visit the manufacturing site and assess the level of compliance with GMP.

Detailed, structured preparation goes into all audits. The procedures for the preparation of audits are set out in Standard Operating Procedures (SOPs) used by the TGA. The SOPs contain detailed information about audit team composition, auditors' responsibilities and audit preparation and notification of audits.

The considerable work that goes into audit preparation, enables the auditors to target certain areas of GMP (that may present higher risks) for examination during the audit.

Monitoring and reviewing audits, auditors and audit outcomes

The TGA also has a number of mechanisms for monitoring and reviewing the performance of audits, the quality of auditors' reports and all audit outcomes.

This is critical in order to ensure consistency in audit practice, accountability and appropriate outcomes. Such monitoring and review is an important part of overall risk management.

For example:

- a range of SOPs have been developed and implemented to guide auditors in their conduct of audits. These SOPs are subject to ongoing review by a dedicated Quality Manager;

- all audits are reviewed by an Audit Manager and may also be referred to a Review Panel for consideration;

- the Chief Auditor (or the designated alternative auditor eg the blood auditor) receives all files relating to problem reports and recalls;

- annual internal audits of the TGA's Quality System for audits are undertaken in order to verify that requirements specified in the Quality System have been implemented effectively, that actual activities comply with these specified requirements and that they are suitable to achieve objectives;

- internal audits of the performance of GMP auditors against established procedures are conducted to determine whether or not they comply with established written procedures; and

- all auditors are subject to ongoing training requirements.

Part D: Medical devices

Section I: Background

As for medicines, the TGA adopts a risk based approach to the assessment of medical devices that involves identification, analysis and evaluation of risks (with subsequent application of treatment options).

However, the actual means by which the TGA implements this is different for medical devices than for medicines.

In 2002, the TGA introduced a new system for the regulation of medical devices, through amendment of the TG Act. The new system incorporates accepted best practice relating to safety, quality and risk management procedures and adopts the philosophies of the Global Harmonisation Taskforce on medical devices.

The new regulatory system utilises the following features:

- a rule-based classification scheme that classifies devices in terms of the risk posed in use;

- compliance with essential principles of quality, safety and performance of the medical device that all devices must meet. Compliance with the essential principles ensures that the product performs the way the manufacturer intends and that the benefits outweigh the residual risk (ie acceptable performance);

- application of a conformity assessment procedure encompassing quality management systems applied to design and manufacturing processes

and requiring an increasing level of independent assessment as the risk profile of the device increases;

- options as to how compliance with the essential principles can be satisfied and assessed (eg manufacturer quality systems, type testing and design evaluation);

- the use of recognised standards to demonstrate compliance with the essential principles;

- a comprehensive post market surveillance and adverse incident reporting program;

- appropriate regulatory controls for the manufacturing processes of medical devices; and

- the continued use of the ARTG as the central point of control for the legal supply of medical devices in Australia.

Section II: Identifying, analysing and evaluating risks posed by medical devices

The new regulatory framework adopts a classification system to categorise medical devices into 5 classes according to the level of risk posed (Class I, Class IIa, Class IIb, Class III and Active Implantable Medical Devices – AIMD).

The system uses a set of classification rules based on a combination of criteria:

- manufacturer's intended use;
- degree of invasiveness in the human body;
- location of use;
- duration of use; and
- use in conjunction with a power supply.

Each criteria has established thresholds. As higher thresholds are exceeded a higher class is assigned.

An assessment is made to ensure that the design, manufacture and performance of the device conforms with the essential principles of safety and performance, essentially ensuring that any risks of using the product are outweighed by the benefits gained.

Essential principles

The essential principles of safety and performance apply to all medical devices. The risks of using a medical device must be outweighed by the benefits gained from the use of the medical device.

The essential principles, detailed in Schedule 1 of the Therapeutic Goods (Medical Devices) Regulations 2002, list the requirements for all medical devices. There are two main categories of essential principles:

- General Principles. These apply to all devices. The General Principles include the following:
  - the use of a medical device must not compromise health and safety;
  - the design and construction of a medical device has to conform with safety principles;
  - medical devices are to be suitable for the intended purpose;
  - long term safety;
  - medical devices are not adversely affected by transport or storage; and
  - the benefits of medical devices are to outweigh any side effects.
- Principles about Design and Construction. The applicability of the principles dealing with design and construction will depend on the intended purpose and properties of the medical device:
  - chemical, physical and biological properties;
  - infection and microbial contamination;
  - construction and environmental properties;
  - medical devices with a measuring function;
  - protection against radiation;
  - medical devices connected to or equipped with an energy source;
  - information to be provided with medical devices; and
  - clinical evidence.

The essential principles set out the requirements relating to the safety and performance characteristics of medical devices.

Compliance with applicable medical device standards is not required, but it is one way to establish compliance with the essential principles. If a manufacturer applies a medical device standard, or a number of medical device standards, this will allow a presumption of conformance with the relevant essential principles. Medical Device Standards Orders (MDSOs) identify applicable standards which can be used to allow presumed compliance. Other standards can also be used to show conformance with the relevant essential principles, however these will not allow an ‘automatic’ presumption of compliance.

In summary, the essential principles have been developed in accordance with international best practice and compliance with such principles ensures that quality is built into the manufacture and supply of medical devices minimising the risks posed to consumers.

Conformity assessment

The classification of a medical device determines the conformity assessment procedure(s) a manufacturer can choose to demonstrate that the device conforms to the particular requirements (ie the relevant essential principles).

The level of involvement of the TGA in conformity assessment is greater for higher risk medical devices than for lower risk medical devices. For example:

- for some low risk medical devices, conformity assessment may take the form of self-certification by the manufacturer. In such cases the manufacturer ensures that the device complies with the relevant essential principles and prepares documentation that allows the conformity to be assessed. The manufacturer may then prepare a declaration of conformity for the medical device and submit this to the TGA;

- for certain high risk medical devices, manufacturers may choose to implement a full quality management system taking into account the regulatory requirements for the design, production, packaging, labelling, and final inspection processes (and include a post-production phase monitoring system). An assessment of the quality assurance system must be made by the TGA (and will be subject to ongoing surveillance audits) before a declaration of conformity may be prepared; or

- other manufacturers of high risk medical devices may choose to undergo type testing for their devices. In such cases, a representative sample of the type of the device (the 'type') has to be examined by the TGA (or other appropriate body) to determine if the design of the type satisfies the essential principles through testing. If the type testing is certified, the manufacturer must seek further certification for the production and final inspection and testing of the device, or have each batch certified.

The declaration of conformity for a given medical device must be available to the product sponsor before an application can be made to have a medical device included in the ARTG. There is a separate part of the ARTG for medical devices, distinct from the parts for registered goods and listed goods.

A sponsor wishing to make an application to have a medical device included in the ARTG must use the Devices Electronic Application Lodgement system (DEAL). DEAL is used to lodge details of the certification held by a medical device manufacturer before an application can be submitted.

All Australian manufacturers of devices are required to hold a conformity assessment certificate issued by the TGA before an application may be made to enter the devices from that manufacturer onto the ARTG (except for very low risk devices where the legislation allows self-certification of compliance with the regulatory requirements).

In addition, overseas manufacturers of certain high risk medical devices must hold a conformity assessment certificate issued by the TGA prior to supply of the devices in Australia, regardless of any certification that they may hold from other regulatory authorities. The types of devices are specified in the legislation and include:

- devices with a medicinal component;
- devices containing material of animal origin that has been rendered non-viable;
- devices that contain material of microbial or recombinant origin; and
- devices that incorporate stable derivatives of human blood or plasma.

Application audits

Using the DEAL process for most correct applications for the inclusion of lower risk medical devices in the ARTG will result in an 'automatic' inclusion, provided evidence of third party assessment (from another regulatory jurisdiction) of the manufacturing processes and in some instances products assessment, have been previously provided. In addition, certain lower risk devices that are subject to self-certification, will result in 'automatic' inclusion. This means that there will not be any further assessment of the application by the TGA prior to the devices being included in the ARTG.

However, applications to higher risk medical devices in the ARTG must be selected for an application audit (based on requirements in the legislation).

In addition, the TGA may select any other application to undergo an application audit. Such audits provide an additional level of risk assessment and treatment by the TGA.

Application audits confirm that the manufacturer of a medical device has carried out the conformity assessment procedures appropriate to the class of the medical device. The audit may consider a range of issues within the application, including whether:

- the device fits the definition of medical device (in the TG Act);
- the device has been correctly classified;
- there is satisfactory evidence that the manufacturer has demonstrated that the device conforms to the essential principles;
- the applicant holds sufficient documentary evidence or has procedures in place to substantiate conformance; and
- the advertising material conforms to any advertising requirement for the device.

If all aspects of the audit are satisfactory, the applicant will be notified, and the medical device will be included in the ARTG. If the decision is not to include the medical device in the ARTG, the TGA will state reasons for the decision when the applicant is notified.

Part E: Blood and tissues

Section I: Regulation of blood

Blood, blood components and plasma derivatives are regulated under the TG Act. Plasma derivatives are regulated as prescription medicines and are therefore subject to the risk identification and treatment processes outlined under Part B of this Chapter.

Some blood and blood components are exempt from TGA oversight to allow for autologous and directed donations under the supervision of a medical practitioner where the blood or blood components are immediately supplied for a named patient on a pre-determined basis.

However, where storage occurs and supervision of that storage by the same medical practitioner can not be guaranteed, the blood or blood components may not be exempt. In such cases the manufacturer of blood or blood components must be licensed in accordance with the Australian Code of GMP for Human Blood and Tissues.

As blood and blood components are not required to be entered into the ARTG, the potential risks relating to these products are managed through GMP audits and licensing of manufacturers. The risk assessment and treatment processes for ensuring compliance with GMP requirements are essentially the same as outlined in Part C of this Chapter.

Section II: Regulation of tissues

Currently, therapeutic products that utilise cells and tissues are subject to differing regulatory requirements, based on the level of risk posed:

- whole organs for transplant are exempt from the legislation (that is, they are defined not to be therapeutic goods at all);

- tissue for implantation in the human body that is obtained, stored and supplied without any deliberate alteration to its biological or mechanical properties is exempt from the requirements for entry on the Register provided that the institution complies with the Code of GMP for Blood and Human Tissues (ie similar requirements as for blood and blood components). Such tissues are those that are generally held in tissue

banks, such as heart valves, skin, corneas and bone. The risk assessment and treatment processes for ensuring compliance with GMP requirements are essentially the same as is outlined in Part C of this Chapter;

- cell and tissue products that are custom made for a particular person (in the case of devices) or medicines that are dispensed, or extemporaneously compounded, for a particular person for therapeutic application to that person are exempt from the requirements for pre-market approval (entry on the Register);

- similarly, those people that have traditionally developed such custom made products are also exempt from the TGA's requirements for licensing of manufacturers – for example:

  - medical practitioners and health care workers are exempt from licensing requirements (and therefore compliance with the cGMP) provided that the "manufacture" of the cell or tissue product is for a patient under his or her care; and

  - biomedical engineers, radiochemists and pharmacists in public hospitals are also exempt from licensing requirements provided that the goods produced are for supply in hospitals or public institutions in the same State or Territory; and

- human tissue and cell extracts, whose principle therapeutic purposes are achieved through chemical, pharmacological, or metabolic actions that are generally able to be batch released, are regulated as medicines and are subject to the risk assessment and treatment processes outlined under Part B of this Chapter. This is because such products pose potentially greater risk.

Given the varying regulatory requirements for blood and tissue products, the following Chapter on monitoring and review focuses only on medicines and medical devices, as the relevant processes discussed are also generally applicable to those blood and tissue products that are included in the ARTG (as either medicines or devices).

CHAPTER 5: MONITORING AND REVIEW

Part A: Background/Context

The TGA shares responsibility for post-market risk assessment and management with sponsors, manufacturers, healthcare providers and patients.

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

For example:

- Sponsors of therapeutic goods have formal obligations under the TG Act to report adverse drug reactions to the TGA.

- Manufacturers of therapeutic goods are regularly re-audited to enable the TGA to monitor their manufacturing processes to ensure that quality is maintained. As part of their Quality Control processes, manufacturers must constantly sample and test the therapeutic goods that they produce and adopt release procedures which ensure that the necessary and relevant tests are carried out, and that materials are not released for use, nor products released for sale or supply, until their quality has been judged satisfactory.

- Medical practitioners, pharmacists, other healthcare practitioners and retailers of therapeutic goods are not compelled under the legislation to report adverse reactions to the TGA but do so on a voluntary basis (they may also report to the sponsor of the therapeutic goods who, in turn, would report to the TGA).

- Consumers generally report serious reactions to health professionals who in turn report to the TGA. In some cases, reports are made directly to the TGA.

- The TGA adopts a number of different post-market risk assessment approaches to ensure the continued safe supply of medicines and medical devices.

Part B: Monitoring and review of medicines

In addition to internal monitoring of TGA processes and practices, there are a number of ways in which the TGA monitors compliance by sponsors and manufacturers of medicines.

For example, the TGA monitors compliance through:

- monitoring adverse events reporting;
- sample testing by the Therapeutic Goods Administration Laboratories (TGAL);
- review of safety related information;
- random and targeted product monitoring of the Electronic Listing Facility for listed medicines;
- desk-top reviews of randomly selected products (listed products);
- full safety and efficacy reviews of products and substances;
- monitoring of medicines problem reports;
- ongoing GMP auditing of manufacturers or ensuring GMP evidence supporting GMP clearance is current;
- review and response to intelligence and tip-offs;
- recalls; and
- surveillance.

The purpose of these post-market monitoring activities is to enable the timely identification, analysis and evaluation of any risks associated with the formulation, manufacture, labelling and advertising of products once they have entered the market-place.

As a result of this monitoring, information might be identified that leads to a re-evaluation of the risks posed in a particular case. Such re-evaluation may be undertaken by:

- a product Regulator;
- an expert Committee such as the Adverse Drug Reactions Advisory Committee;

- GMP auditors; and/or
- a combination of these.

Evaluation of the risks enables the TGA to identify any additional treatment options that may be necessary (or any other changes to the treatment approach previously adopted).

This is the broad context within which the TGA undertakes systematic risk management.

A structured risk management approach is also applied by each of the areas responsible for each of the different post-market activities.

For example:

- In relation to ***sample testing by TGAL***, a risk management approach drives the work of the laboratory. Risk assessment enables the identification of products for targeted and routine testing. Sampling plans are developed based on a risk assessment. The plans include detailed information such as:

  - the class/product categories to be tested;
  - the products themselves or identifying characteristics;
  - the tests to be undertaken;
  - the justification/reasons for the testing; and
  - the risk that the products pose.

  Like the GMP audit schedules, the sampling plans are also subject to ongoing monitoring and review and revisions are made as changes to risk profiles are identified.

- In relation to ***desk-top review of randomly selected listed products,*** a sampling methodology was developed by the TGA (with the assistance of the ABS) based on an expected 10% proportion of applications with errors, a required precision of +/- 4% and a 95% confidence interval. Based on an average of 700 applications for listing per quarter this means that approximately 172 applications for listing are subject to a Level 1 Review per quarter (688 per year). Of these, a number of samples are required to submit additional information for Level 2 Review. Of these, some are also required to submit additional information for a Level 3 Review.

- In relation to ***GMP auditing,*** the TGA schedules audits based on risk. The risk profile for a particular manufacturer is developed taking into account a number of factors. From information obtained from these risk factors the TGA determines the period between audits (eg the audit schedule and the relative priority accorded to the audit of different manufacturers) and the most appropriate means for undertaking the audit (for example, announced or unannounced).

- In relation to ***monitoring adverse events,*** where problems with a product are identified by the TGA, a risk analysis is undertaken by the relevant product regulator. This involves consideration of the significance of the hazard, the channels by which the goods have been distributed and the level to which distribution has taken place (as detailed in the Uniform Recall Procedures for Therapeutic Goods). The product regulator may also consult with the sponsor, the Australian Recall Co-ordinator, TGA scientists and clinical advisers, external experts, expert committees and professional bodies.

  SOPs require the TGA to document information about the product defect including the source of the risk, the consequences, the likelihood of occurrence, the level of risk and the overall risk assessment. The action to be taken must also be detailed (including reasons for the action taken) and the proposed action must be authorised by the relevant Section Head (all cases), the Branch Director (for most recalls) and the Medical Officer (in the case of safety related recalls). This process ensures that the risks are properly identified and evaluated and that the appropriate treatment action (level of recall) is applied.

Part C: Monitoring and review of medical devices

Once a medical device has been approved for supply in Australia it is necessary to make sure that the product continues to meet all the regulatory, safety, and performance requirements and standards that were required for the approval.

This is in addition to making sure that any problems (or risks) associated with the problem are dealt with and reported through appropriate channels.

There are three main components of post-market activities for medical devices. The components are:

- the manufacturer's post-market surveillance system;
- post-market monitoring of market compliance by the TGA; and
- vigilance programs.

Manufacturer's post-market surveillance system

All manufacturers of medical devices must implement and maintain a post-market monitoring system to seek and assess information concerning the performance of devices after supply. The post-market surveillance system requires manufacturers to:

- systematically review experiences gained after the medical device was supplied in Australia;

- implement corrective action, commensurate with the nature and risks involved with the medical device; and

- notify the sponsors of the medical device of adverse events and near events.

Information feeding into the system can come from many different sources including expert user groups, customer surveys, literature reviews and user reactions.

The Australian Medical Device Guidelines (Guidance Document Number 11 – Post-market activities) provides detailed information for sponsors and manufacturers about sponsor's and manufacturer's 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); and

- reporting exemption rules.

Post-market monitoring of market compliance by the TGA

Post-market monitoring by the TGA is a series of activities carried out to ensure the ongoing regulatory compliance and safety of medical devices supplied to the Australian market and to take action when this does not occur.

Monitoring activities may include:

- audits of technical and clinical information to show compliance to the essential principles;

- inspections of manufacturer's or sponsor's records and documentation;

- on-site tests or taking samples for off-site testing;

- testing or auditing to confirm compliance with the essential principles;

- audits of distribution records;

- audits of the traceability of raw materials used in the manufacture of therapeutic goods and tracking of component parts; and

- audits of compliance with GMP requirements.

Vigilance programs

Vigilance programs are a range of activities undertaken by the TGA and the manufacturer or sponsor after any party becomes aware of any of the following in relation to medical devices:

- adverse events (notification and evaluation of adverse events is known as the Medical Devices Vigilance System);

- malfunctions;

- results of testing; or

- other information.

All adverse events, regardless of whether they have to be reported under the vigilance system, are expected to be included in the manufacturer's post-market system.

The combination of monitoring activities detailed above enables the TGA to identify any additional treatment options that may be necessary (or any other changes to the treatment approach previously adopted).

CHAPTER 6: ENFORCEMENT ACTION

If new risks have been identified (or previously identified risks have been realised through, for example poor manufacturing processes or a break down in quality systems), the TGA then has a number of different means for treating such risks.

The TGA's enforcement options are detailed in the therapeutic goods legislation and include the capacity to:

- impose new conditions on the registration or listing or vary or remove existing conditions;
- apply additional conditions to the manufacture of the product;
- cancel the registration or listing of the product, meaning it can no longer be supplied in Australia;
- suspend or cancel a manufacturing licence;
- require mandatory recalls of products; or
- investigate alleged breaches with a view to briefing the Director of Prosecutions to pursue a prosecution under the legislation (which may result in the imposition of monetary fines or imprisonment terms).

The enforcement action selected will depend on the particular circumstances of the case. Of course the dominant consideration of the TGA must always be the protection of the health and safety of the public.

CHAPTER 7: COMMUNICATION AND CONSULTATION

Part A: Background/Context

Communication and consultation are important at each step of the risk management process.

Effective internal and external communication is important to ensure 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.

Part B: Communication and consultation within the TGA

As mentioned previously, the overall system of risk assessment and risk management within the TGA involves a number of different players within the TGA with a range of different skills and experience.

All of the different areas within the TGA work together to provide each other with information and resources to enable them to undertake well informed risk assessments.

There are a number of formal and informal channels through which the Regulators within the TGA communicate including:

- through Standing Committees that oversee the Corporate Governance of the TGA. These include:
    - the TGA National Manager's meeting. The committee comprises all Branch Heads within the TGA and meets weekly to report on program activities and hot issues and share information on general issues. This enables any organisational risks to be identified and communicated regularly. The members are expected to provide feedback from the meeting to their Section Heads/Team Leaders and any other appropriate staff.
    - the TGA Corporate Governance Group. The focus of this committee is on strategic and corporate management issues of significance. Among other things, the Group considers and endorses strategic level plans including Corporate and Business

Plans, develops and oversights human resource management policies and practices, oversees the implementation of recommendations arising from organisation reviews, monitors spending and agrees the allocation of financial resources. The Group meets monthly. Committee members are expected to convey the outcome of each meeting to their Section Heads/Team Leaders.

- Therapeutics Policy and Planning Committee. The role of this Committee is to consider issues related to the regulation of therapeutic goods including making decisions on all new policy proposals and proposals for legislative change. The Committee also monitors the implementation of such legislation and oversees the implementation of major program-specific, cross-program and management strategies

- regular Section Heads meetings for the Branch Head to pass on to the Section Heads the above information as well as any other information or events of significance;

- regular Section meetings for the Section Head to pass on to staff the above information and discuss issues relevant to the work of the Section; and

- meetings every three months between the National Manager and all Section Heads and Branch Heads of the TGA to share information on major issues within the TGA;

- the generation of quarterly performance reports and provision of these to all areas of the TGA; and

- shared access to databases, including the Laboratory Information Management Systems (LIMS), the TGA Recalls and Medicine Problem Reporting mainframe databases and Strategic Information Management Environment (SIME).

In addition to these formal mechanisms, the different functional areas of the TGA also communicate any significant problems to each other and, if necessary, arrange meetings to discuss appropriate action(s).

Part C: Communication and consultation with external stakeholders

The TGA implements a number of measures to ensure that the TGA's stakeholders are well informed about developments within the TGA, are well educated about the TGA's requirements and are provided the opportunity to provide feedback to the TGA.

- ***Industry*** - Consistent with good regulatory practice, the TGA believes that effective communication with manufacturers is the key to ensuring strong compliance. To this end, the TGA:

  - meets with industry and consumer representatives on both a multi- and bilateral basis throughout the year. For example, the TGA meets bilaterally with each industry group to provide a strategic briefing on work plans for the coming year and to seek information on likely impacts for that sector. At the meeting the TGA presents an update on the current year's budget and business plan and discusses performance information. The TGA seeks input from industry on regulatory and performance issues and engages them in discussion on trends and emerging issues;

  - holds meetings of the TGA Industry Consultative Committee (TICC) involving all industry sectors and consumer representatives;

  - holds regular bilateral meetings between each regulator and representatives of their industry sector with discussion centred on matters of specific interest;

  - writes to industry associations seeking feedback on any proposed changes to policy, legislation and Codes/standards;

  - includes detailed information on the website (including TGA news, consultation documents etc);

  - regularly presents at conferences of peak bodies. Through these conferences the TGA can communicate information to stakeholders, gain information on changes to the industry (and key issues affecting the industry) and also seek informal feedback on the TGA's activities;

  - holds seminars whenever there are significant changes to legislation, requirements, Codes/standards etc; and

  - offers industry the opportunity to call, email or meet with TGA staff at any time.

Industry bodies are also represented on a number of the TGA committees. Communication and consultation continually feeds into the risk management process.

- ***Healthcare practitioners*** – in addition to being represented on TGA committees, the TGA is regularly in contact with healthcare practitioners to, among other things, encourage them to report on adverse events. The main means by which the TGA communicates with health practitioners is through peak bodies, through the TGA website and through the TGA's involvement in conferences and forums involving healthcare practitioners.

- ***State and Territory governments*** – as a national regulatory scheme, State and Territory governments have a direct interest in, and involvement in, the TGA's administration of the scheme.

  State and Territory governments play a policy role through forums such as the Health Ministers Advisory Committee and the Australian Health Ministers Conference. The TGA holds formal twice yearly meetings with State and Territory representatives through the National Co-ordinating Committee on Therapeutic Goods (NCCTG). The NCCTG also holds additional meetings on an as-needs basis.

  States and Territories also play a practical role in implementation of the regulatory requirements for therapeutic goods. For example, each State and Territory has a State Recall Co-ordinator that assists the TGA with the recall of products.

- ***International regulatory bodies*** – the TGA has agreements with a number of overseas regulatory bodies to enable the TGA to recognise certificates of GMP compliance issued by regulatory bodies that have an equivalent regulatory system. In order for this approach to operate effectively, close communication between the TGA and the other international regulators is critical. The TGA ensures such communication through informal means (such as regular teleconferences and visits) and through more formal means such as representation on, or involvement with, peak international bodies.

- ***The community*** – the primary means by which the TGA communicates with the public is through the TGA website. The TGA website notifies the public of any inquiries that are being undertaken by the TGA and any opportunities for comments on Discussion Papers or regulatory proposals. The TGA also receives consumer input through representation of consumers on peak TGA committees including, for example, the Expert Committee on Complementary Medicines. In situations where the recall of a product is necessary the TGA ensures that all relevant information is available to consumers

CHAPTER 8: SUMMARY

In summary, risk assessment and management underpins all aspects of the work of the TGA in regulating therapeutic goods.

It is not simple to describe the approach because it is multi-dimensional, involving a range of different players and a number of different areas of the TGA each applying a risk management approach to different aspects of their work.

As discussed in this document:

- there are many different sources of risk associated with therapeutic goods including the product itself, the way that the product is manufactured, the way the product is prescribed and the way the product is used by the patient;

- all participants in the medical product development and delivery system 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. Risk assessment and management occurs at each of these levels and by all participants in the system;

- the role of the TGA is to, among other things, develop and implement appropriate national policies and controls for therapeutic goods that provide some assurance that products supplied in Australia are safe, of high quality and efficacious.

- in fulfilling its role, the TGA adopts a risk management approach. Throughout the agency, different areas are applying risk assessment and management models to different aspects of their work.

- For example:

    - risk assessment informs whether a product is registered or listed on the ARTG which in turn informs the level of pre-market evaluation undertaken by the TGA;

    - risk assessment underpins the TGA's pre-market evaluation of registrable medicines;

    - risk assessment drives the post monitoring activity undertaken by the TGA including, for example, the scheduling of GMP audits, the sampling of products for testing by the TGA laboratories and the selection of products and substances for post-market review of safety and efficacy;

- a risk management approach underpins the system of approvals administered by the TGA (whether this be licensing of manufacturers or entry of products on the ARTG). The treatment option imposed by the TGA is that which is necessary to manage the risks;

- a risk management approach underpins the TGA's undertaking of enforcement action;

- constant monitoring and review, not just of therapeutic goods themselves, but also of the TGA's processes and practices, provides the TGA with ongoing information about how risks can be better managed. This enables the TGA to implement a comprehensive "whole of agency" approach to continuous improvement; and

- communication and consultation within the TGA and with external stakeholders ensures that there is a continuous feedback loop and that information from a very wide variety of sources is available to the TGA to assist it in its role in risk assessment and management of medicines.