# Description of a possible joint regulatory scheme for therapeutic products under ANZTPA

January 2013

# FOREWORD

In June 2011, the Australian and New Zealand Governments announced their agreement to proceed with a joint scheme for regulation of therapeutic products (that is, medicines, medical devices, biological and others) to be administered by the Australia New Zealand Therapeutic Products Agency (ANZTPA).

As the Heads of the current regulatory agencies in Australia and New Zealand, TGA and Medsafe, we are now inviting participation in discussion of the high level aspects of a possible framework for regulation of therapeutic products under the joint agency.

The possible framework has been developed against the background of the Trans Tasman Mutual Recognition Arrangement that aims to develop a more integrated trans-Tasman economy by removing regulatory impediments between Australia and New Zealand and to enable goods to be traded freely between them. It is also based on the Treaty, an Agreement between the Government of Australia and the Government of New Zealand for the establishment of a joint scheme for the regulation of therapeutic goods, signed by both countries in 2003.

The objective is to develop a responsive and cost-effective regime for regulating therapeutic products that is consistent with international best practice.

This discussion paper on a possible framework has been released on the Transition to ANZTPA website with the intention that responses will inform both governments as the ANZTPA project moves forward. Submissions are invited to address the key aspects of the framework and the likely impact on stakeholders. Submissions should be received by 21 February 2013.

This is the start of a conversation with stakeholders. We will continue to engage with stakeholders over the coming months as, subject to final decisions of both governments, we work to finalise draft legislation and develop the detail of the regulatory scheme and its associated business processes. We have a unique opportunity to shape the thinking around the design and operation of the new regulatory scheme and the new regulator ANZTPA. In doing so, we want to draw on the strengths of our current regulatory approaches and learn what we can and should do differently and better.

We encourage you and your organisation to consider the outlined proposals and to provide comments and input to guide the future development of a regulatory scheme under ANZTPA that will benefit consumers, industry, health professionals and governments in both Australia and New Zealand.

If you have any question please do not hesitate to contact the ANZTPA Project team at anztpa.info@anztpa.org

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# INTRODUCTION

The Governments of Australia and New Zealand have expressed a commitment to advancing a single economic market under which differences arising from policies and regulations of both countries will be minimised or removed, thereby reducing transaction costs for consumers, business and governments and providing for a more seamless market.

As part of this commitment the Trans Tasman Mutual Recognition Arrangement (TTMRA), an agreement between the Commonwealth of Australia, the states and territories of Australia and New Zealand, entered into force in 1998. The objective of the TTMRA is to allow goods produced in Australia to be traded in New Zealand and vice versa. At present, mutual recognition of therapeutic goods has not been achieved and they are exempt from the requirements of the TTMRA.

In December 2003 the Australian and New Zealand Governments signed a Treaty[1] ("*Agreement between the Government of Australia and the Government of New Zealand for the Establishment of a Joint Scheme for the Regulation of Therapeutic Products*") outlining a joint regulatory scheme for therapeutic products to be administered by a joint agency, the Australia New Zealand Therapeutic Products Agency (ANZTPA). The Treaty addresses Australia's and New Zealand's obligations under the TTMRA to work together to develop a more integrated trans-Tasman economy by removing regulatory impediments between the two countries and to enable goods to be traded freely between them. It provides a framework for the joint regulatory scheme and also sets out the governance and accountability arrangements for the new regulatory agency. Negotiations on the scheme contained in the Treaty were postponed in 2007 after it became apparent that the New Zealand implementing legislation could not be progressed at that time. On 20 June 2011, the Australian and New Zealand Prime Ministers reaffirmed their commitment to closer economic relations by signing a "Statement of Intent" on a plan to establish ANZTPA and to progressively implement the joint regulatory scheme for therapeutic products (as described in the Treaty) over a period of five years. The Statement of Intent acknowledges that the New Zealand Government will introduce a separate scheme to regulate natural health products in the New Zealand market.

The joint scheme will consist of implementing legislation of the Australian and New Zealand Parliaments, Rules made by a Ministerial Council consisting of the Australian Minister for Health and the New Zealand Minister of Health, and Orders made by the Managing Director of ANZTPA.

The implementing legislation will deal with matters such as the making of the Rules and Orders, offences and civil penalty provisions to support the regulatory requirements in the Rules, enforcement powers, administrative law and judicial review matters and the governance and accountability of ANZTPA. ANZTPA will be established in accordance with the Treaty and established as a body corporate by the Australian implementing legislation. The Rules will contain the "business-as-usual" for ANZTPA as described in this

[1] http://www.anztpa.org/historical/treaty.htm

document including provisions about product approvals and manufacturing licences. Orders will cover matters such as standards.

In accordance with the statement of intent, the joint regulatory scheme is scheduled to come into operation on 1 July 2016 by which time the implementing legislation will be in operation in each country and the Ministerial Council Rules and the Orders will be in force.

**This paper describes the contents of a possible regulatory scheme for therapeutic products in Australia and New Zealand to be administered by ANZTPA. For ease of reading, it is written actively as if the scheme would be implemented in the form described. However, this is not necessarily the case. The paper is intended as a "conversation starter" – it provides the public, industry, consumers, health care professionals and other stakeholders with information about the content of a possible scheme for comment and input.**

**The regulatory scheme described in the paper should not be taken as reflecting the final form of the joint scheme for introduction under ANZTPA. Further work will be required before the detailed operation of the scheme is defined and settled. The scheme's final form will be determined by the Australian and New Zealand Governments after consultation with all relevant parties.**

Issues such as the scheduling of medicines and ANZTPA's involvement in the regulation of the advertising of therapeutic products are not described in this paper and will be the subject of further development and consultation.

The content of a possible scheme described in this paper takes as its starting point the draft ANZTPA Rules in relation to which consultation took place in 2006 prior to the 2007 postponement of the previous Australian-New Zealand negotiations. The inclusion of sunscreens, biologicals and *in vitro* diagnostic (IVD) products within the scope of the scheme reflects the intended coverage in 2006, as does the exclusion of disinfectants from the scheme.

Where relevant, more recent regulatory reforms including those outlined in the TGA Blueprint[2], such as those related to regulation of medical devices and complementary medicines, will be incorporated into the ANZTPA scheme. Stakeholders in New Zealand and Australia are encouraged to participate in the consultation processes that will be occurring in the context of the TGA Blueprint Reforms programme.

**Readers should be aware that in the period leading to 2016, the Australian and New Zealand governments might agree additional reforms to the regulatory scheme. These would be subject to consultation with stakeholders.**

The purpose of the joint regulatory scheme is to ensure appropriate regulatory controls for therapeutic products manufactured and/or supplied in Australia and New Zealand and

[2] See *TGA Reforms: A blueprint for TGA's future* at http://www.tga.gov.au/about/tga-reforms-blueprint.htm.

exported from Australia or New Zealand. It is expected the scheme will do this in a manner consistent with international best practice, by setting out particular requirements for suppliers and manufacturers of therapeutic products and providing for enforcement of those requirements through a series of offences and civil penalty provisions.

This will be achieved through a scheme that:

- is responsive and cost-effective
- applies a level of regulation that is commensurate with the potential risks to public health and safety posed by therapeutic products
- balances these risks and the potential benefits to be obtained by users from the availability of these products in Australia and New Zealand
- ensures consumers and health professionals have sufficient, accurate information to enable them to select and use therapeutic products safely and effectively
- assists New Zealand and Australian states and territories to adopt a uniform approach to controlling consumer access to therapeutic products
- as far as possible, harmonises requirements with overseas regulators of equivalent standard.

In describing and developing a regulatory scheme for therapeutic products, it should be acknowledged that therapeutic products have a "life cycle," starting with research and development, through to regulatory approval, and finally use in the "real world." ANZTPA will provide appropriate regulatory oversight of therapeutic products in both the pre- and post-market phases of their life-cycle.

The TGA and Medsafe will engage with interest groups over the next few weeks about this paper. If you would like to provide written comments you can find out more about how to do so at the ANZTPA.org website at www.anztpa.org .

# MEDICINES

Under the joint regulatory scheme, it is proposed that a medicine will be defined in a way that will include the following product types:

- prescription medicines
- 'over-the-counter' (OTC) medicines
- 'complementary medicines'
- most medical gases
- vaccines
- allergens
- biotechnology medicines
- plasma products, including immunoglobulins
- radiopharmaceuticals
- most radio-contrast agents
- dialysis solutions, except haemodialysis solutions
- sunscreens.

Medicines will be regulated by ANZTPA using a risk-based approach that is consistent with best international practice and is built around the following key elements:

- compliance with standards
- ensuring manufacturers operate in accordance with manufacturing principles
- product approval
- post-market monitoring and surveillance.

## Separate regulation of certain, low-risk "natural health and supplementary products" in New Zealand

The New Zealand Government is introducing a separate scheme to regulate certain natural health products, for example dietary supplements, herbal remedies and traditional medicines. On 31 October 2012 the New Zealand Health Committee reported to the New Zealand Parliament on the Natural Health Products Bill and recommended by majority that the Bill be passed with amendments. The full report can be obtained from the New Zealand Parliament website[3].

The New Zealand natural health and supplementary products scheme will be reviewed five years after commencement and the review will consider whether or not to maintain a separate scheme for these products that would otherwise be covered by the ANZTPA joint scheme.

[3] Located at http://www.parliament.nz/en-NZ/PB/SC/Documents/Reports/0/9/f/50DBSCH_SCR5643_1-Natural-Health-Products-Bill-324-2.htm.

# STANDARDS

ANZTPA will be able to determine standards for medicines to be set out in Orders and relating to:

- the quality of medicines and ingredients in medicines
- the manufacture of medicines
- containers, closures and packaging
- presentation of medicines
- information for consumers and healthcare professionals, including product labels
- terminology to be used in applications and in information for consumers or healthcare professionals
- other matters concerning the quality, safety and efficacy of medicines.

Medicines would need to conform to all relevant standards, except with the written consent of ANZTPA. In determining standards, ANZTPA may consult with the relevant expert advisory committee specifically established to advise on standards.

Standards determined by ANZTPA in Orders would have priority over other applicable standards.

The Rules will provide for a list of ANZTPA-approved sources of monographs[4] ("default" Standards) to apply to medicines in circumstances where no other specific standard is prescribed.

# MANUFACTURE OF MEDICINES

The manufacturing and quality control of medicines for supply in or export from Australia and/or New Zealand will be required to be of an acceptable standard.

## Manufacturing principles

The criteria used to assess and determine standards of manufacture will be set out in manufacturing principles, which will be determined by ANZTPA and set out in Orders.

Manufacturing principles may relate to any of the following:

- the standards to be maintained, and premises and the equipment to be used, for the manufacture of medicines
- procedures for quality assurance and quality control to be employed in the manufacture of medicines

[4] Monographs specifying tests and standards for ingredients and finished dosage forms are contained within reference texts such as the British Pharmacopoeia, the European Pharmacopeia and the United States Pharmacopeia.

- the qualifications and experience required of people employed in the manufacture of medicines
- the manufacturing practices to be employed in the manufacture of medicines
- other matters relevant to the quality, safety and efficacy of medicines that are manufactured in Australia or New Zealand.

## Manufacturing licences

Australian and New Zealand manufacturers of medicines will be required to hold a manufacturing licence granted by ANZTPA unless exempted from this requirement.

## Obtaining a manufacturing licence

To obtain a manufacturing licence, the manufacturer will need to submit an application to ANZTPA. The application will need to:

- identify the medicines or classes of medicine that the applicant proposes to manufacture
- identify the premises where the medicines will be manufactured
- identify the steps in manufacture that the applicant proposes to carry out
- state the names, qualifications and experience of the people who will control the production of the medicines and the quality control measures that are to be employed.

ANZTPA will be able to obtain additional information from the applicant and may require the applicant to allow an authorised person to inspect the manufacturer's quality assurance system and the premises, equipment, processes and facilities that will be used to manufacture medicines.

A manufacturing licence will be granted if ANZTPA is satisfied that:

- the applicant will be able to comply with the manufacturing principles
- the premises are satisfactory for the manufacture of the medicines
- the applicant and anyone else with significant involvement in the manufacture is a 'fit and proper person'.

A manufacturing licence will relate to a particular manufacturer and manufacturing site(s), specified step(s) in manufacture and specified type(s) of medicine.

## Imposition of conditions on a manufacturing licence

ANZTPA will be able to impose conditions on a manufacturing licence. A manufacturing licence will be granted subject to standard conditions including the following:

- that the medicines conform to any applicable standards

- that the manufacturing principles are observed in carrying out any steps in the manufacture of medicines under the licence
- appropriate records are kept relating to the manufacture of the medicine and they are retained for a specified period after the expiry date of the batch of medicine to which they relate
- authorised persons are allowed to enter the manufacturing premises, to inspect the premises, the medicines and any of the substances used in the manufacture and to take samples or copy documents etc.

In addition to the standard conditions, ANZTPA will be able to impose specific conditions on a manufacturing licence at the time it is granted, or subsequently, and may also vary or remove existing conditions.

## Suspension or revocation of a manufacturing licence

ANZTPA will be able to revoke a manufacturing licence or suspend a licence for a specified period of time if, for example, a condition of the licence is breached or the licence holder, or anyone else who has significant involvement in the manufacture, is not a fit and proper person.

In certain circumstances, ANZTPA will be able to revoke or suspend a licence without giving notice (for instance at the request of the holder or in exceptional circumstances). Otherwise ANZTPA will be required to give the licence holder an opportunity to make submissions in relation to any proposal to suspend or revoke the licence.

## Validity of a manufacturing licence

Consideration is being given to whether:

- once issued, a manufacturing licence will remain valid for a specified period (unless suspended or revoked during that time) to be reissued for a further specified period based on satisfactory compliance and inspection history; and
- the manufacturer should be required to make annual declarations that the details relating to the licence remain correct.

ANZTPA will be able to vary the terms of a manufacturing licence as a result of its consideration of a renewal application or as a consequence of an inspection. As noted above, it will have power to impose, vary or remove conditions on the licence at any time.

## Exemption from manufacturing licensing

Certain medicines or classes of medicines will be exempt from the requirement to be manufactured by a licensed person. While no final decisions have been made on the

therapeutic products that will be exempt, they are likely to be similar to those currently exempt in Australia.[5]

Additionally, certain persons will be exempt from the requirement to obtain a manufacturing licence when manufacturing specified medicines in specified circumstances but subject to any applicable conditions. Again, though no final decisions have been made, they are likely to be similar to the circumstances in which manufacture is currently exempt in Australia.[6] .

## Overseas manufacturers

If a person wishes to seek approval to supply a medicine in Australia or New Zealand and some or all of the steps in the manufacture of that medicine have been carried out in a place outside Australia and New Zealand then the person seeking the product approval must supply evidence to ANZTPA that each manufacturer involved has acceptable manufacturing and quality control procedures in place.

ANZTPA will consider whether the overseas manufacturer complies with the manufacturing principles and if satisfied will issue a document indicating that the particular manufacturer has the clearance to perform those steps in manufacture specified in the document. The clearance will be granted for a specified period.

ANZTPA will reserve the right to undertake an inspection of an overseas manufacturing site, irrespective of any other evidence supplied. An inspection could take place prior to initial clearance being given or at any time after.

# PRODUCT APPROVALS

A medicine covered by the joint scheme will only be able to be:

- imported into Australia or New Zealand
- exported to a third country from Australia or New Zealand
- supplied in Australia or New Zealand,

by the holder of a product approval granted by ANZTPA, unless specifically exempted.

A person intending only to export a medicine from Australia and/or New Zealand to a third country will be able to obtain a special type of approval, an 'export-only approval'.

ANZTPA will grant (or refuse) a product approval on the basis of a submitted application. Depending on the nature of the medicine and the purpose for which it is used, an

[5] These include antiperspirant preparations that derive their antiperspirant properties from inorganic salts of aluminium, zinc or zirconium only, medicated soaps other than liquid medicated soaps, dentifrices that contain no therapeutically active substance other than not more than 1000 milligrams per kilogram of fluoride and bulk, liquefied medical gases.

[6] For example, current exemptions in Australia include radiochemists and pharmacists in public hospitals in relation to the manufacture of therapeutic goods by the person when employed by a public hospital or a public institution and produced by that person for supply in hospitals or public institutions in the same state or territory and pharmacists manufacturing therapeutic products in their own pharmacy ('extemporaneous compounding') or in a private hospital for supply from those premises only.

application may be based on certifications made by the applicant, whereas in other cases comprehensive data will need to be submitted to support the application for it to be approved.

As a general principle, a product approval application for a medicine will need to demonstrate that the potential risks to those for whom medicine is intended to be used are outweighed by the therapeutic benefit of the medicine.

In general, any changes to the medicine that represent a change to the information upon which the granting of the approval was based will need to be the subject of an additional application and be authorised by ANZTPA before they can be implemented.

A register of product approvals will be maintained by ANZTPA.

## Classification of medicines

Medicines intended for supply in Australia and/or New Zealand will be classified as either Class 1 medicines or Class 2 medicines. The classification will determine the product approval procedure that applies to the medicine.

The classification of a medicine will be based on a number of factors, including:

- the intrinsic risk of the product (e.g. the toxicity of its ingredients)
- the risks associated with the quality of the product (e.g. requirements for sterility)
- the risks associated with the intended use(s) of the product.

Class 1 medicines will be low risk and the product approval procedure will be based on certifications made by the applicant and an automated validation of key data by ANZTPA. ANZTPA will be able to conduct post-approval audits to check that applicant certifications were, and remain, correct. It is expected that the medicines that are currently regulated as 'listed complementary medicines' in Australia will be Class 1 medicines.

Class 2 medicines will be higher risk and the product approval procedure will be based on a pre-market evaluation of the quality, safety and efficacy of the medicine undertaken by ANZTPA. However, within this class there is a continuum of risk and the product approval process and data requirements applying to a Class 2 medicine will be commensurate with the risks associated with the individual medicine.

If a medicine is incorporated in a medical device, then the safety and quality of the medical device will need to be verified in accordance with the requirements for medical devices, and the ancillary action of the device must be verified having regard to the intended purpose of the medicine, before an approval could be granted.

### *Class 1 medicines*

In order to satisfy ANZTPA that a medicine is a Class 1 medicine with overall low risks on the basis of all contributing risk factors, the medicine:

- must contain only ingredients included on a published list of permitted ingredients and comply with any relevant requirements set out in the list

- must not contain certain types of ingredients, (e.g. ingredients that are scheduled as prescription medicines, pharmacist-only medicines or pharmacy medicines or that meet the requirements for such scheduling)
- must not be required to be sterile[7]
- must only carry indications permitted by ANZTPA (which will generally not include indications about the treatment of certain kinds of disease, disorders or conditions)
- must only carry indications and make claims that are supported by evidence held by the applicant which, in the case of indications, meet certain evidence requirements.

Sunscreen preparations that meet specified criteria[8] will be Class 1 medicines as will other 'low risk' medicines that meet criteria set out in the Rules, e.g. medicated throat lozenges.

Lists of ingredients and indications permitted for Class 1 medicines will be developed. For ingredients, this list will be based on the ingredients currently permitted in listed medicines in Australia. For indications, the list will be developed prior to implementation of the joint scheme.

It will be possible for a person to apply to have a substance added to the list of ingredients permitted for use in Class 1 medicines. In evaluating such an application, ANZTPA will have regard to whether the substance:

- is of acceptable quality
- meets the requirements for not being scheduled as a prescription medicine, pharmacist only medicine or pharmacy medicine
- is safe as an ingredient for use in Class 1 medicines considering its likely use.

Following evaluation of the application by ANZTPA, a decision will be made to approve or reject the application. ANZTPA may attach conditions or other requirements in relation to the use of the substance in Class 1 medicines.

ANZTPA will publish and maintain the permitted ingredients lists.

It will also be possible for a person to apply to have indications added to the list of indications permitted by ANZTPA to be used in relation to Class 1 medicines.

### *Class 2 medicines*

A medicine will be a Class 2 medicine unless it:

- meets the criteria for classification as a Class 1 medicine or
- is an export-only medicine.

[7] Irrespective of formulation or intended purpose, if a medicine is required to be sterile, it cannot be a Class 1 medicine.

[8] Generally sunscreen preparations with an SPF > 4.

### *Export-only medicines*

Medicines intended only for export from Australia and/or New Zealand to a third country will be classified as 'export-only' medicines.

## The product approval

A product approval will be valid in both Australia and New Zealand, i.e. it will permit the medicine that is the subject of the approval to be imported into, exported from and supplied in both Australia and New Zealand.

A product approval will remain valid provided annual charges are paid and the approval is not suspended or revoked.

## Obtaining a product approval

To obtain a product approval for a new medicine, an application will need to be submitted to ANZTPA. The applicant must have a presence in Australia or New Zealand.

Depending on the type of medicine, ANZTPA will assess the application before a decision is made to grant (or to refuse) a product approval. The data requirements and the application and evaluation fees payable will depend on the classification of the medicine. Relevant factors in determining the data requirements of an application will include:

- whether the medicine contains a new active substance or is a generic medicine
- the intended use(s) of the medicine
- the proposed dosage form(s) and route(s) of administration
- whether the medicine only contains ingredients that have been approved by ANZTPA and makes only certain kinds of claims
- whether the application is for a "variation" to a medicine that is currently approved but the variation creates a "separate and distinct" medicine
- the likely scheduling of the medicine.

### *Class 1 medicines*

For Class 1 medicines, the product approval application will need to contain certifications by the applicant, including that:

- the medicine conforms to every standard (if any) applicable to the medicine
- the medicine contains only ingredients that have been approved by ANZTPA
- the indications in relation to the medicine are only those that are permitted by ANZTPA
- it is manufactured by a person with a manufacturing licence (if in Australia or New Zealand)

- if a step in the manufacture of the medicine has been carried out outside Australia or New Zealand, ANZTPA must have certified that the manufacturing and quality control procedures used in each such step are acceptable
- the presentation of the medicine is not unacceptable
- all relevant advertising requirements are complied with
- the applicant holds information or evidence to support any indication and claims made in relation to the medicine and that the evidence in relation to the indications meets relevant evidence requirements.

On receipt of an application for approval of a Class 1 medicine, ANZTPA will grant an approval if the application is complete and requisite certifications have been made and key data in the application have been validated.

At any time after an approval has been granted for a Class 1 medicine, ANZTPA may audit the application to determine whether any or all the matters certified by the applicant were and remain correct.

### *Class 2 medicines*

The data requirements for an application for approval of a Class 2 medicine will vary depending on the risk of the medicine.

In evaluating the application, in addition to ensuring that relevant standards and manufacturing principles have been met, ANZTPA will have regard to whether the quality, safety and efficacy of the medicine for the purposes for which it is to be used have been satisfactorily established, acknowledging that the concepts of safety and efficacy must be judged in relation to each other and in accordance with the state of contemporary relevant scientific knowledge.

ANZTPA will make a decision to grant or to refuse any approval for a Class 2 medicine on the basis of evaluation of the application and may seek advice from a relevant expert advisory committee before making a decision.

Where the application is for a 'variation' to an approved Class 2 medicine and that variation creates a 'separate and distinct product,' ANZTPA may require only certifications or an abbreviated data package be provided by the applicant.

### *Export-only medicines*

Exporters of export-only medicines will be required to obtain an export-only approval. The export-only approval system will be designed to:

- ensure that export-only medicines meet appropriate quality and safety standards, consistent with ANZTPA's international public health obligations
- ensure that ANZTPA has in its records the particulars required to provide export certifications for export-only medicines
- ensure that, in the event of a safety concern related to a particular substance, manufacturer or supplier, ANZTPA is able to readily and rapidly identify all

medicines at risk, whether supplied in Australia or New Zealand or exported to a third country and take appropriate action

- minimise the regulatory impost on exporters of medicines, recognising that, in many importing countries, medicines exported from Australia and/or New Zealand will be subject to relevant local regulatory requirements.

In order to obtain an approval for an export-only medicine, the exporter will be required to submit to ANZTPA an application that includes certifications in relation to the medicine. These will include, but may not be limited to, certifications that:

- the medicine will not be supplied in Australia or in New Zealand
- the medicine is safe for the purposes for which it is to be used
- the medicine conforms to every standard (if any) applicable to the medicine
- if the medicine has been manufactured in Australia or New Zealand, each step in the manufacture of the medicine has been carried out by a licensed manufacturer
- either the applicant holds information or evidence to support any claim that the applicant makes relating to the medicine or the applicant has a written agreement with the importer of the medicine in the destination country, which states that the importer is responsible for substantiation of any claims made in relation to the medicine
- either the applicant holds data to demonstrate that the product specifications will continue to be met for the period of the shelf life under the nominated storage conditions or the applicant has a written agreement with the importer of the medicine in the destination country, which states that the importer is responsible for nominating the shelf life of the medicine
- the medicine does not contain a substance the exportation of which is prohibited under Australian or New Zealand Customs legislation
- the medicine meets all relevant regulatory requirements in the destination country.

If a step in the manufacture of the medicine has been carried out outside Australia or New Zealand, the applicant must obtain from ANZTPA a certificate that the manufacturing and quality control procedures used in each such step are acceptable.

ANZTPA will be required to select an application for an export-only approval for a pre-approval audit in particular circumstances (for instance where an approval for supply in Australia or New Zealand has been refused) and will have power to do so in other circumstances.

After an approval has been granted for an export-only medicine, ANZTPA would be able to audit the application to determine whether any or all the matters certified by the applicant were and remain correct.

## Provisional approval

Consideration is still being given for ANZTPA, in exceptional circumstances, when it considers it appropriate to grant a provisional approval for a medicine. A provisional product approval for a medicine would be for a time-limited period and subject to conditions and further evaluation of the medicine prior to completion of the provisional authorisation period.

Applicants would be required to lodge a standard application for approval of a product. Provisional approval could be granted where there was insufficient safety or efficacy information to justify the granting of a full approval if ANZTPA determined that there was an overriding clinical need for the medicine to be available. Provisional approvals would only be granted for medicines to be used in the prevention or treatment of life-threatening illnesses and where the medicine was likely to provide clinically significant therapeutic benefits to patients over existing treatments. This would allow limited access to a medicine where the potential benefit is considered greater than the risk of non-treatment.

## Statutory timeframes for some approval applications

Statutory timeframes would apply to applications for the approval of Class 2 medicines. Consideration of the application would need to be completed within the relevant timeframe or a proportion of the evaluation fee would be refunded.

## Conditions of approval

The granting of an approval will be subject to certain standard conditions set out in the Rules. Additionally, ANZTPA will be able to impose conditions on an approval at the time it is granted, and could impose new conditions or vary existing conditions on an existing approval.

## Standard conditions

Standard conditions along the lines of the following are expected to apply to all approved medicines.

- The approval holder must not advertise the medicine for an unapproved indication.
- The approval holder must allow authorised persons to enter any premises to inspect those premises and medicines at those premises and to take samples of medicines or ingredients of medicines.
- The approval holder must produce documents relating to the medicines or their ingredients and allow an authorised person to copy the documents.
- The approval holder must keep records relating to the medicine necessary to:
    - expedite recall of any batch of the product
    - identify the country(ies) to which each batch of the product was exported

    - identify the manufacturer(s) of each batch of the product.
- If requested to do so by ANZTPA, the approval holder must supply a reasonable number of samples of a medicine for testing purposes.
- The approval holder must provide information about overseas regulatory action.
- If the particulars for a medicine are proposed to change the approval holder must apply to ANZTPA (see further below).
- All steps in the manufacture of the medicine are undertaken by a licensed manufacturer or one that has manufacturing and quality control procedures in place that are acceptable.

It will also be a condition of approval that approval holders comply with pharmacovigilance requirements as well as an offence not to report certain types of adverse events.

In addition to the above, it would be a standard condition for Class 1 medicines that the approval holder hold and retain information or evidence to support any indication or other claims in relation to the medicine throughout the period of approval and provide it to ANZTPA on request.

In addition to the above, standard conditions along the lines of the following are expected to apply to the approval of all export-only medicines.

- Where the approval holder for an export only medicine has certified that they have a written agreement with the importer of the product in the destination country, the approval holder will provide a copy of the agreement to ANZTPA on request.
- The approval holder shall not export any export-only medicine for supply after the expiry date of the batch of the product.

## Specific conditions

In addition to the standard conditions, ANZTPA will be able to impose specific conditions on an approval. It will also be able to impose specific conditions on an existing approval or vary or remove existing conditions at its own initiative or at the request of the approval holder.

Conditions could relate to:

- the manufacture of the medicine
- the custody, use, supply, disposal or destruction of the medicine
- the keeping of records relating to the medicine
- matters dealt with in standards applicable to the medicine
- the advertising of the medicine
- specific pharmacovigilance or risk management activities which may include training and education and additional reporting requirements.

Normally conditions imposed by ANZTPA would relate to all batches of the product that are the subject of the approval. However, ANZTPA will be able to impose conditions that relate only to specific batches of the product.

If the imposition or variation of conditions is necessary to prevent imminent risk of death, serious illness or serious injury, they would have immediate effect. Otherwise there would be a statutory minimum period before which the changes came into effect unless the change was the result of request by the approval holder.

## Variations to an approval

As noted above, it will be a condition of an approval that relevant changes to an approved medicine will need prior authorisation from ANZTPA.

Where changes to an approved medicine would result in the creation of a new, separate and distinct medicine, an application for a new approval will be required (though, depending on the circumstances, it may be done through a certification or abbreviated process). Otherwise, changes would be treated as variations to an existing approval.

On receipt of a variation application for a Class 1 medicine, ANZTPA would vary the approval if the application was complete (including certifications if relevant) and the change did not create a separate and distinct medicine.

In the case of an application to vary the approval of a Class 2 medicine, ANZTPA will have to make a decision as to the appropriateness of the requested variation.

If the only effect of the variation was to reduce the class of persons for whom the product is suitable or to add a warning or precaution, and ANZTPA was satisfied that the variation requested did not result in an unacceptable presentation, ANZTPA would vary the approval. In other cases, ANZTPA would need to be satisfied that there was no reduction in the quality, safety or efficacy of the medicine for the purpose of which it is intended to be used.

Consideration is being given to a mechanism whereby, in certain circumstances (where the nature of the proposed variation is low risk), an application to vary an approval for a Class 2 medicine could be approved on the basis of certifications made by the applicant. In general, the applicant would certify certain matters in the variation application including that they hold evidence to support the change and that they will provide that evidence to ANZTPA if requested to do so. ANZTPA will be able to audit such 'self-certified' variations. This is similar to what is currently done administratively by the TGA for certain kinds of low risk variations to registered medicines.

### *Variations to approvals for export only medicines*

On receipt of a variation application for an export-only medicine, ANZTPA could vary the approval if the application was complete and the change did not create a separate and distinct medicine.

***Statutory timeframes for variation applications***

ANZTPA will be required to deal with some variations to Class 2 medicines within statutory timeframes.

## Data protection

When evaluating an application for approval of a new Class 2 medicine, ANZTPA will not be able to use 'protected information' relating to another medicine. Details of the arrangement are yet to be finalised but information is likely to be protected information if:

- the information was given to ANZTPA (or Medsafe or the TGA) in relation to an application to approve a medicine (the existing medicine) consisting of, or containing, an active component
- the information is about the active component and is not available to the public
- when the application to approve the existing medicine was lodged:
    - no other medicine consisting of, or containing, that active component was approved
    - no such medicine had been approved at any time before then
    - five years had not passed since the day the existing medicine was approved
- the person in relation to whom the existing medicine was approved had not given ANZTPA (Medsafe/TGA) permission in writing for ANZTPA to use the information.

## Revocation and suspension of approvals

ANZTPA will be able to suspend or revoke an approval in the event that the approval holder fails to comply with relevant regulatory requirements, including the conditions of approval, or ANZTPA receives information on the safety, quality or efficacy of the medicine that makes such an action necessary.

## Automatic revocation of approval

ANZTPA will be required to revoke an approval if the approval for the medicine had been suspended and the period applying to the suspension expired before the suspension was revoked. Likewise ANZTPA will be required to revoke an approval if it becomes apparent that protected information was used in evaluating the medicine for approval.

## Revocation of approval with immediate effect

In certain circumstances, ANZTPA will have the power to revoke an approval with immediate effect, in which case the person who held the approval must immediately cease import, supply or export of the product. If necessary, the product may also be recalled.

ANZTPA will be able to revoke an approval on a range of grounds, including where:

- there would be imminent risk of death, serious illness or serious injury if the medicine continues to be supplied
- the approval holder does not comply with a direction or requirement in relation to advertising
- the product contains substances that are prohibited imports for the purposes of the Australian and/or New Zealand Customs legislation
- the approval holder has refused or failed to comply with the conditions of the approval relating to the manufacture of the product, record-keeping requirements, or the requirement to allow authorised persons to enter and inspect premises, take samples and view and copy documents
- a manufacturer of the medicine has failed to comply with the manufacturing principles.

In addition to the above circumstances applying to all medicines, ANZTPA will be able to revoke an approval for a Class 1 medicine with immediate effect if, for example, the approval holder fails to supply information for the purpose of ascertaining whether the medicine should have been approved, the medicine is not in fact a Class 1 medicine or there is a serious breach of the requirements relating to advertising and, as a result of the breach, the presentation of the medicine is misleading to a significant extent, or the medicine contains ingredients that are not permitted.

In addition, ANZTPA will be able to revoke (with immediate effect) an approval for an export-only medicine if, for example:

- it appears that the approval holder has incorrectly certified that each step in the manufacture of the medicine has been carried out by a person who is the holder of a licence to carry out that step, or
- the approval holder fails to comply with a request from ANZTPA for information or documents for the purpose of ascertaining whether the medicine should have been approved.

## Revocation of approval after notice of proposal to revoke

Where the grounds for revoking an approval without notice (ie with immediate effect) do not exist, ANZTPA will be required to notify the approval holder of the intention to revoke the approval and give the holder the opportunity to make submissions in relation to the proposed action. Before making a decision on a proposal to revoke an approval, ANZTPA will be required to consider any such submissions.

ANZTPA will be able to revoke an approval for a medicine (following a notice of proposal to revoke) for a range of grounds including where:

- the safety, quality or efficacy is unacceptable
- the goods have changed such that they are now a 'separate and distinct good'
- an approval condition has been breached

- the approval holder has not complied with its reporting obligations in relation to adverse events
- the approval holder fails to provide information when requested to do so by ANZTPA
- the medicine does not comply with applicable standards
- the advertising requirements have been breached in relation to the medicine
- a step in the manufacture of the medicine was not conducted by an appropriately approved manufacturer
- the presentation of the medicine is unacceptable
- the approval holder no longer has the necessary connection with Australia or New Zealand.

ANZTPA will also be able to revoke an approval for an export-only medicine (following a notice of proposal to revoke) if, for example, the exporter has refused or failed to comply with a condition on the approval, the product does not conform to an applicable standard or a step in the manufacture of the medicine was carried out by a person who did not hold a licence to carry out that step.

ANZTPA will be also able to revoke an approval for a Class 1 medicine or an export-only medicine (following a notice of proposal to revoke) if it appears that any of the certifications made by the applicant in the approval application are incorrect.

## Suspension of an approval

Suspension of an approval will stop further import, supply, export or promotion of a product pending provision of additional information by the approval holder to enable ANZTPA to determine whether or not the approval should remain valid or be revoked.

ANZTPA will be able to suspend an approval for a medicine if satisfied that there is a potential risk of death, serious illness or serious injury if the medicine continues to be supplied and it is likely that, within the period of the suspension, the approval holder will be able to take the action necessary to rectify the situation.

ANZTPA will also be able to suspend an approval if it is likely there are grounds for the revoking of the approval.

The period of suspension cannot exceed a specified statutory period (likely to be six months). However, the suspension may be extended (for a limited period specified in the Rules) if the approval holder is able to show that he/she has taken steps to remove the grounds for suspending the approval.

# MEDICAL DEVICES

The purpose of a regulatory scheme for medical devices is to assure the safety and satisfactory performance of medical devices supplied in Australia and New Zealand or exported from Australia or New Zealand.

Under a possible joint regulatory scheme, a ***medical device*** may be defined as:

> *any instrument, apparatus, appliance, material or other article (whether used alone or in combination, and including the software necessary for its proper application) intended, by the person under whose name it is or is to be supplied, to be used for human beings for the purpose of one or more of the following:*
>
> *i. diagnosis, prevention, monitoring, treatment or alleviation of disease;*
> *ii. diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability;*
> *iii. investigation, replacement or modification of the anatomy or of a physiological process;*
> *iv. control of conception;*
> *v. disinfection of medical devices;*
>
> *and that does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but that may be assisted in its function by such means.*

It should be noted that an accessory to a medical device would be regulated as a medical device. Also, ANZTPA will have the ability to declare a product to be, or not to be, a medical device.

Australia is currently considering a range of reforms to medical device regulation as part of the Blueprint reforms[9] and following the Review of Health Technology in Australia report[10] and the two recent reports of the Senate Community Affairs Reference Committee on regulatory standards for the approval of medical devices[11] and on the role of the TGA regarding medical devices, particularly Poly Implant Prothese (PIP) breast implants[12].

Reforms under consideration include the following:

- increasing the level of pre-market assessment of implantable and surgically invasive medical devices intended for long-term use
- increasing the level of transparency of TGA decisions in relation to medical device applications
- changing the types of medical devices manufactured in Australia that require a TGA conformity assessment certificate.

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9 See *TGA Reforms: A blueprint for TGA's future* at www.tga.gov.au/about/tga-reforms-blueprint.htm.
10 Located at www.health.gov.au/internet/main/publishing.nsf/Content/hta-review-report.
11 Located at http://www.aph.gov.au/Parliamentary_Business/Committees/Senate_Committees?url=clac_ctte/completed_inquiries/2010-13/medical_devices/report/index.htm
12 Located at http://www.aph.gov.au/Parliamentary_Business/Committees/Senate_Committees?url=clac_ctte/completed_inquiries/2010-13/implants_2012/report/index.htm .

These proposals for reform are subject to a separate consultation process being undertaken by the TGA. New Zealand as well as Australian stakeholders are encouraged to participate in those consultation processes.

Subject to further developments in relation to those reforms, the key features of the possible joint regulatory scheme for medical devices will be:

- product approvals as the central point of control for the importation and supply of medical devices in Australia and New Zealand
- prescribed essential principles for the quality, safety and performance of the medical device that must be complied with before the product can be supplied
- a device classification scheme based on different levels of risk for each class of device
- a choice of conformity assessment procedures that can be used by manufacturers to demonstrate initial compliance and on-going compliance with the essential principles
- the use of recognised standards to satisfy the requirements of the essential principles
- a comprehensive post market surveillance system including compliance testing, adverse event reporting and appropriate regulatory controls for the manufacturing processes of medical devices
- mechanisms of access to unapproved devices
- a framework for the regulation of *in vitro* diagnostic (IVD) devices as a subset of medical devices.

The ***manufacturer*** of a medical device is the person who is responsible for the design, production, packaging and labelling of the device before it is supplied.

A manufacturer of a medical device, may also be the person, who, with a view to supplying the device, performs one or more of the following actions using ready-made products - assembles, packages, processes, refurbishes or labels the device or assigns the device its purpose by means of information supplied. However, a person is not the manufacturer if the person adapts an already supplied medical device for the use of an individual patient.

## Classification of medical devices

Medical devices will be classified by the manufacturer according to the intended purpose of the medical device and the degree of risk involved to the patient and the user. The device classifications will be determined using a set of rules which take into account the level of invasiveness in the human body, duration and location of use and whether the device is powered or not.

The classification of a medical device determines the conformity assessment procedure(s) a manufacturer can apply in order to demonstrate an adequate level of control over manufacture and design of the device. The classification also determines the level of regulatory oversight of the manufacturer's conformity assessment procedures.

The four risk classifications of medical devices will be those currently used in Australia and will be based on internationally agreed criteria such as those recommended by the Global Harmonisation Task Force (GHTF)[13]:

- Class I (low risk)
- Class IIa (low-medium risk)
- Class IIb (medium-high risk)
- Class III (high risk, including active implantable medical devices).

All medical devices will be subject to a level of scrutiny under the joint regulatory scheme that is commensurate with their risks to individual and public health. Higher-risk devices will undergo a more stringent form of conformity assessment than lower risk devices.

## Conformity assessment and the essential principles

In order to gain an approval to supply a medical device in Australia and New Zealand, an applicant must be able to demonstrate to ANZTPA that the device complies with a set of essential principles. These essential principles will set out requirements relating to the safety and performance of medical devices. A principles-based framework, rather than prescriptive requirements, allows for technological advances in medical devices and will provide flexibility for manufacturers.

There will be six general essential principles that apply to all devices and a further nine essential principles about design and construction that will apply to devices on a case-by-case basis, depending on the intended purpose and technology used in the medical device.

***General principles that will apply to all devices***

- Use of medical devices not to compromise health and safety
- Design and construction of medical devices to conform to safety principles
- Medical devices to be suitable for intended purpose
- Long-term safety
- Medical devices not to be adversely affected by transport or storage
- Benefits of medical devices to outweigh any side effects

***Particular principles about design and construction***

- 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

13 The duties of the GHTF have now been taken over by the International Medical Devices Regulators' Forum (IMDRF).

- Information to be provided with medical devices
- Clinical evidence
- Principles applying to in vitro diagnostic (IVD) medical devices only

The means by which a manufacturer can demonstrate that they have met the essential principles will not be mandated. Nevertheless, as part of demonstrating compliance with the essential principles, the manufacturer will need to have the necessary conformity assessment certification to determine that the medical device is safe and performs as intended. In order to gain the necessary conformity assessment certification, manufacturers must comply with a minimum set of conformity assessment procedures which will be defined and based on the level of risk of the device.

The level of assessment required by ANZTPA at the point of application will depend on the following:

- the risk classification of the device
- who issued the conformity assessment certificate
- whether there are any concerns with the application that would require further information to be provided by the applicant.

This system of review will be consistent with consistent internationally agreed frameworks such as that previously recommended by the GHTF.

# MANUFACTURE OF MEDICAL DEVICES

## Conformity assessment procedures

'Conformity assessment procedure' is the term used to define the pre-market process that a manufacturer of medical devices needs to follow in order to demonstrate compliance with regulatory requirements. It will be an essential part of the approval of medical devices by ANZTPA.

In essence, the application of a conformity assessment procedure required for a medical device is commensurate with the level and nature of risk posed by the medical device to the patient or user. This will range from manufacturer self-assessment, for the lowest risk medical devices, through to implementation of a full quality management system for manufacture and development of a product design dossier, to demonstrate compliance with the essential principles, for the highest risk devices.

As part of the conformity assessment procedures, the manufacturer will be required to make a 'declaration of conformity' which requires a statement that the medical device is classified correctly and complies with the applicable provisions of the essential principles. ANZTPA will be able to review and assess how the conformity assessment procedures were applied.

Special conformity assessment procedures will apply to medical devices that are for particular purposes, for instance those intended for special and experimental use or custom-made devices for a medical practitioner or a specific patient.

## Conformity assessment standards

Medical device standards for products and conformity assessment standards for manufacturing or quality management system processes will be determined by ANZTPA and set out in Orders. Compliance with these Orders will not be mandatory, but will be one way to establish compliance with essential principles. Other ways, including the use of other relevant standards, may be used to demonstrate compliance with the essential principles.

To claim compliance with a medical device standard or a conformity assessment standard, the device must fall within the scope of the standard and the requirements of the standard must be explicitly applied.

## Issuing of conformity assessment certificates

All manufacturers, except manufacturers of Class I medical devices, will be required to hold evidence that the application of the conformity assessment procedures has been assessed for compliance by an appropriate regulatory body. This evidence is in the form of a conformity assessment certificate. Manufacturers of Class I medical devices may self-declare compliance. At the present time, Australian manufacturers must hold a conformity assessment certificate issued by the TGA. Certification issued by other bodies is not accepted. Consideration is being given to whether third party conformity assessment bodies could issue conformity assessment certificates for some medical devices.

ANZTPA will have the authority to issue a conformity assessment certificate to a manufacturer for a particular medical device. The certificate will signify one or more of the following:

- relevant quality management systems and manufacturing processes required by the conformity assessment procedures are in place
- compliance with the essential principles for the device
- compliance with other requirements of the conformity assessment procedures.

Currently in Australia, certification issued to overseas manufacturers by European Conformity Assessment Bodies (also known as Notified Bodies) is accepted for most medical devices, since the Australian and European regulatory requirements are very similar. Acceptance of European certification is subject to mandatory review of a sub-set of the technical documentation for high-risk devices, and random or targeted review for lower risk devices. The manufacturer must provide a Declaration of Conformity to the Australian requirements, to show that the conditions of use in Australia, and any differences in the regulatory requirements, have been considered.

The Australian and New Zealand Governments each have a Mutual Recognition Agreement (MRA) with the European Community; under which certification issued to European manufacturers by certain European Notified Bodies is accepted, except for a subset of high risk devices (such as those containing tissues of animal origin or medicines). Under these, or similar, MRAs it is anticipated that ANZTPA will continue with these arrangements and

will be able to assess Australian and New Zealand manufacturers for compliance with the European requirements allowing the manufacturer to affix a CE mark for supply in Europe.

Depending on the risk classification of the device, a conformity assessment certificate may be required before a valid application can be made for approval to supply the medical device.

Conformity assessment certificates will not be required for low risk (Class 1) medical devices that are not intended to be sterile or that do not have a measuring function or any medical device that is exempt from the requirement.

The decision to issue a conformity assessment certificate will depend on an assessment of the quality management system, where required, and satisfactory demonstration of compliance with the essential principles. A conformity assessment certificate will specify whether it covers all medical devices manufactured by the manufacturer or only specified medical devices.

When a conformity assessment certificate is issued to a manufacturer of a medical device by ANZTPA, standard conditions will be imposed on the certificate. Breaching any of these conditions may lead to the suspension or revocation of the certificate. Additionally, ANZTPA may impose special conditions on a conformity assessment certificate at the time it is issued or subsequently and may also vary or remove existing conditions.

Once issued, a conformity assessment certificate will remain valid for a specified period, if any.

## Revocation or suspension of a conformity assessment certificate

ANZTPA will have the power to revoke a conformity assessment certificate or suspend a certificate for a period of time. In certain circumstances, a conformity assessment certificate could be revoked with immediate effect.

If a conformity assessment certificate is revoked with immediate effect, the import, supply or export of the product must immediately cease. In certain circumstances, the product may also be recalled.

Where the circumstances for revoking a certificate without notice (ie with immediate effect) do not exist, ANZTPA will have to advise the manufacturer of the intention to revoke the certificate and give the manufacturer the opportunity to make submissions in relation to the proposed action.

A conformity assessment certificate may be suspended pending provision of additional information by the manufacturer to enable ANZTPA to determine whether or not the conformity assessment certificate should remain valid or be revoked. Medical devices covered by the suspended certificate would not be able to be supplied during the period of suspension.

# PRODUCT APPROVALS

A medical device may only be

- imported into Australia or New Zealand
- exported to a third country from Australia or New Zealand
- supplied in Australia or New Zealand

by the holder of an approval issued by ANZTPA, unless specifically exempted.

A person intending only to export a medical device from Australia and/or New Zealand to a third country may obtain a special type of approval, an "export-only" approval.

Approvals will be granted on the basis of an application submitted to ANZTPA; the application will be required to include certifications made by the applicant, a copy of the manufacturer's declaration of conformity and, where required, a conformity assessment certificate. The applicant will need to have a presence in Australia or New Zealand.

Depending on the classification of the device, a product approval for a medical device would usually be issued automatically once a complete application is submitted with the required certifications and declarations. However, applications for some kinds of devices will always, and applications for other kinds of devices may, be selected for an application audit by ANZTPA, which would involve a check of some or all aspects of the application and certification.

In order to maintain a product approval, the approval holder must ensure there are no significant changes by the manufacturer to any of the information upon which the conformity assessment certification was issued. If significant changes by the manufacturer are made, these must be subject to further assessment and approval.

A register of product approvals will be maintained by ANZTPA.

The register of product approvals will include particulars such as:

- the approval holder
- the manufacturer
- the device nomenclature code
- the medical device classification
- the unique product identifier (where relevant)
- the intended use of the kind of medical device
- the conditions subject to which the approval is granted.

When ANZTPA issues a product approval for a medical device, a unique approval number will be assigned.

## Kind of medical device

Generally, a separate approval will be issued for each new "kind of medical device". The circumstances in which a medical device is a new kind of medical device will depend on the type of device, its classification and the nature of the difference or change. Criteria will be used to determine whether medical devices are of the same kind. These criteria will include attributes such as manufacturer, classification and product approval holder.

## Obtaining an approval

To obtain an approval to supply a new kind of medical device, the applicant will be required to certify that:

- the manufacturer has determined that the devices of the kind concerned are medical devices
- the device is intended for a purpose specified by the manufacturer
- the device has been correctly classified by the manufacturer in accordance with the medical device classifications
- the device has been declared to conform with the essential principles, and the applicant is either in possession of sufficient information to substantiate compliance with the essential principles or has procedures in place to ensure that the information can be obtained from the manufacturer within the prescribed timeframe
- an appropriate conformity assessment procedure has been applied to the device and the applicant is either in possession of sufficient information to substantiate the manufacturer's declaration of conformity with the essential principles or has procedures in place to ensure that the information can be obtained within the prescribed time
- the advertising material relating to the device complies with all applicable requirements
- the information included in or with the application is complete and correct
- the applicant is a resident of or carries on business in, Australia or New Zealand.

The manufacturer's declaration of conformity will need to be presented as part of the application process for approval to supply.

## Conditions of approval

Certain standard conditions will apply to all approvals to supply medical devices and in addition conditions can be imposed on approvals for medical devices. These will be appropriate to ensure that the relevant requirements continue to be met throughout the life of the product.

Standard conditions will relate to entry and audit powers, delivery of samples, availability of information and advertising material and the reporting of adverse events. In addition to

the standard conditions, ANZTPA may impose specific conditions as part of the decision to issue an approval. Conditions may be added, varied or removed.

## Variations to an approval

ANZTPA will be able to vary the terms of an approval following a request by the approval holder or at its own initiative.

## Suspension or revocation of an approval

ANZTPA may suspend or revoke an approval in the event that the approval holder fails to comply with relevant regulatory requirements, including the conditions placed on the approval. The approval may also be suspended or revoked if ANZTPA receives information on the safety, quality or performance of the medical device, which makes such an action necessary.

The period of any suspension cannot exceed a specified statutory period (likely to be six months). However, the suspension may be extended (for a limited period specified in the Rules) if the approval holder is able to show that he/she has taken steps to remove the grounds for suspending the approval.

In certain circumstances, an approval could be revoked with immediate effect. Otherwise, the approval holder must be given notice and the opportunity to make submissions about the proposed action. Suspension of an approval would stop further import, supply or export of a product pending provision of additional information by the approval holder to enable ANZTPA to determine whether or not the approval should remain valid or be revoked.

# IN VITRO DIAGNOSTIC DEVICES

In vitro diagnostic medical devices (IVDs) are, in general, 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. IVDs are typically used in diagnostic laboratories, at the point of care, and in the home. Without appropriate regulatory control of IVDs there is potential for inadequate protection of public and personal health.

Under ANZTPA, all IVDs will undergo a level of regulatory scrutiny that is commensurate with the risks associated with their use. The framework will be consistent with internationally agreed frameworks such as that recommended by the GHTF for IVDs, ensuring that requirements are internationally aligned. The framework will provide the flexibility and capacity to regulate new and changing technology.

IVDs will be regulated as a subset of medical devices; however, due to the unique nature of IVDs there will be several points of difference between the regulation of IVDs and other medical devices. There will be a separate classification system for IVDs and some additional essential principles specific to IVDs.

Products intended for general laboratory use that are not manufactured, sold or presented for use as an IVD will not be regulated by ANZTPA. Likewise, the regulatory framework administered by ANZTPA will not cover products that are not intended for therapeutic use in humans, including tests for parentage and kinship, drug tests used in sport, most tests for alcohol or the detection of illicit drugs.

The IVD regulatory framework will have the following features:

- approval by ANZTPA as the basis for legal supply
- compliance with a set of essential principles for the quality, safety and performance of the IVD
- an IVD classification scheme based on different levels of risk for each class of device
- a choice of conformity assessment procedures, based on the risk classification, to be applied by manufacturers to demonstrate initial and on-going compliance with the essential principles
- use of compliance with recognised standards as a means to demonstrate that the essential principles and conformity assessment procedures have been met
- provision for post market activities, including compliance testing, adverse event reporting and recalls
- mechanisms for access to unapproved IVDs in cases of special need.

## Risk classification of IVDs

IVDs will be classified into four classes, based on risk:

- Class 1 IVD (no public health risk / low personal risk)
- Class 2 IVD (low public health risk / moderate personal risk)
- Class 3 IVD (moderate public health risk /high personal risk)
- Class 4 IVD (high public health risk)

Examples of Class 1 IVDs include laboratory equipment intended for use in *in-vitro* diagnostic testing; Class 2 includes IVDs that detect the presence or exposure to infectious agents that do not cause serious disease and IVDs such as pregnancy tests; Class 3 includes IVDs used to diagnose serious infectious diseases or where an erroneous result would put the patient in an imminent life-threatening situation; Class 4 includes IVDs used for testing of the blood supply and organ and tissue donations for pathogens or used for detecting agents used in biological warfare (eg anthrax).

An IVD must be approved by ANZTPA prior to being imported, supplied or exported; however provision will be made for access to unapproved IVDs in certain circumstances, including in the event of a possible or actual emergency.

The requirements for approval to supply by ANZTPA will depend on the risk classification of the IVD, as follows:

**Class 1 IVDs**

The applicant will need to obtain the Global Medical Device Nomenclature (GMDN) from the manufacturer and must declare that the IVD complies with the essential principles. The manufacturer's evidence of conformity must be held but is not required to be submitted to ANZTPA unless requested.

**Class 2 & Class 3 IVDs**

The applicant will need to obtain the GMDN and a copy of the evidence of conformity with the essential principles from the manufacturer and will be required to submit this evidence as part of the application. Australian and New Zealand manufacturers will be required to meet the appropriate manufacturing standards and have their systems certified by ANZTPA.

**Class 4 IVDs**

The applicant will need to obtain the GMDN and a copy of the manufacturer's ANZTPA-issued Conformity Assessment Certificate and will be required to submit this evidence as part of the application.

In addition to the general essential principles applying to all medical devices, there will be seven principles that are specific to IVDs. It will be the manufacturer's responsibility to demonstrate that its IVD complies with the relevant essential principles. Justification will need to be provided for any specific principle that the manufacturer considers is not applicable.

The regulatory framework will include the regulation of in-house IVDs which are developed within a laboratory or laboratory network and are not supplied in a commercial context.

## Issuing of conformity assessment certificates

ANZTPA will be able to issue a conformity assessment certificate to the manufacturer of an IVD if it is satisfied that the appropriate standards have been met. A conformity assessment certificate may be required before a valid application can be made for approval to supply an IVD in Australia and/or New Zealand.

At the present time, a manufacturer who manufactures IVDs in Australia; Class 4 IVDs manufactured outside Australia; or others who do not have appropriate overseas certification, must hold a conformity assessment certificate issued by the TGA. Certification issued by other bodies is not accepted.

## Issuing of approvals

Approvals will be issued for IVDs in the same way as for other medical devices.

## Access to IVDs for home-use

IVDs intended for home-use (i.e. tests not carried out under the supervision of a health-care provider) will be regulated in accordance with the risk class, with particular attention to be paid to instructions for use. However, the following IVDs will be prohibited from home-use:

- those used to test blood and tissues for pathogens or diagnose notifiable infectious diseases
- genetic tests
- those used to test for serious disorders, such as cancer and myocardial infarction.

## IVDs for non-therapeutic use

IVDs for non-therapeutic use such as tests for parentage and kinship, drug tests used in sport and tests for alcohol and illicit drugs will generally fall outside the scope of the joint regulatory scheme for therapeutic products because they are not for therapeutic use.

# BLOOD & BLOOD COMPONENTS

Blood and blood components will be regulated by ANZTPA. Plasma derivatives will be regulated as medicines subject to full regulation under the provisions relevant to Class 2 medicines.

The term 'blood' relates to whole blood extracted from human donors and 'blood components' means therapeutic components that have been manufactured from blood (including red cells, white cells, platelets and plasma). 'Blood components' do not include products derived through fractionation of plasma.

Some blood and blood components will be exempt from regulation by ANZTPA, including blood and blood components that are:

- collected by a medical practitioner in the course of medical treatment and for the purposes of diagnosis of, or testing for, a medical condition
- manufactured by a medical practitioner for therapeutic application to a particular patient under the practitioner's care
- manufactured by a blood collection centre for a medical practitioner for therapeutic application to a particular patient under the practitioner's care.

These exemptions are generally considered to cover autologous[14] 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. Where storage occurs and supervision of that storage by the same medical practitioner cannot be guaranteed, the blood or blood components may not be exempt from regulation by ANZTPA.

A manufacturer of blood or blood components (which are not exempt) must obtain a manufacturing licence and to do this the manufacturer must satisfy ANZTPA that the blood, blood components and/or plasma are manufactured in compliance with the appropriate Code of Good Manufacturing Practice and in a manner consistent with the relevant Technical Master File provided by the manufacturer.[15] ANZTPA will be responsible for determining the standards which must be met and to the extent possible these will be consistent with internationally agreed standards.

Once an appropriate manufacturing licence has been issued by ANZTPA, the manufacturer will be able to supply blood and blood products covered by the manufacturing licence without further product approval. Technical Master Files will be reviewed and manufacturing facilities will be inspected periodically by ANZTPA. The outcomes of these reviews and inspections will need to be satisfactory in order to maintain a manufacturing licence.

14 This is the situation in which the donor and recipient are the same person.

15 'Technical Master Files' are compilations of scientific data which include a description of the steps in manufacture that demonstrate that the blood or blood components are manufactured according to the appropriate standards.

# BIOLOGICALS

Under ANZTPA, a regulatory framework for biologicals will be established to regulate human tissues and cellular therapies. The framework will apply different levels of pre-market regulation to biological products based on the risks associated with the use of each product and will be flexible enough to accommodate emerging technologies. All products within the scope of the framework will need to comply with the relevant product standards and manufacturing principles. These standards will be harmonised with international standards, where possible and relevant.

For the purposes of the regulatory framework, a "biological" will be an item made from, or containing, human cells or human tissues, and that is used to:

- treat or prevent disease or injury
- diagnose a condition of a person
- alter the physiological processes of a person
- test the susceptibility of a person to disease
- replace or modify a person's body part(s).

ANZTPA will have the ability to declare a particular product to be (or not to be) a biological for the purposes of regulation under the joint scheme.

IVDs that contain human cells or tissues will be regulated as IVDs, because these devices are used externally to the patients ('*in vitro*') and so any cells or tissues (biologicals) they contain are not in contact with the people being diagnosed.

The biologicals regulatory framework will provide a comprehensive system of pre-market assessment and controls that must be completed before biologicals are allowed to be supplied in Australia and/or New Zealand, and further post-market controls after they are supplied.

The framework will allow for four classes of biologicals based on the risk posed by the products, which are in turn related to the methods used to prepare and process the products during their manufacture and whether their intended use is the same as their usual biological function. The framework will also include provisions to allow supply of unapproved biologicals under certain circumstances (such as for clinical trials, emergency situations or use by individual patients) and for 'exceptional release' to allow the supply of a specific item or batch that does not meet required manufacturing or product standards under certain clinically urgent circumstances.

Fresh viable human organs or human haematopoietic progenitor cells, for direct donor-to-host transplantation, will be specifically excluded from the regulatory scheme. Also, subject to certain conditions, human tissue and cells collected from a patient and used for the treatment of that same patient will be excluded from the framework. Reproductive tissue (e.g. sperm, eggs, embryos for *in vitro* fertilisation) that are 'unmanipulated' (i.e. they have not been processed in any way apart from freezing) will also be excluded from the framework.

## Risk classification of biologicals

**Class 1 biologicals**

For a biological to be classified as Class 1, the risks associated with the use of the product should be very low, with the risk satisfactorily managed by a high level of clinical oversight e.g. the manufacture is under expert medical supervision. The manufacture of Class 1 biologicals must comply with relevant mandatory standards that will be determined by ANZTPA to ensure the quality, safety and efficacy of the product. ANZTPA will declare which products can be regulated as Class 1 biologicals.

**Class 2 biologicals**

Class 2 biologicals will be products that have undergone no or only simple methods of processing and are for homologous use. *Homologous use* means using cells or tissues from a donor for the repair, reconstruction, replacement or supplementation of a recipient's cells or tissues and where those cells or tissues perform the same basic function in the recipient as in the donor. Examples include human heart valves and corneas.

**Class 3 biologicals**

Class 3 biologicals will be products processed using methods that are considered to alter the cells or tissue beyond minimal manipulation, and may be either for homologous use (replacing like with like), or for functions other than their original, natural function. Class 3 biologicals will include, for example, demineralised bone, cultured fibroblasts for skin repair, and chondrocytes for cartilage repair.

**Class 4 biologicals**

Class 4 biologicals will be products processed in a way that alters their original function and state and include, for example, genetically modified cells.

# MANUFACTURE OF BIOLOGICALS

## Manufacturing licences

A person will need a manufacturing licence issued by ANZTPA to manufacture Class 2, Class 3 or Class 4 biologicals in Australia or New Zealand. A manufacturing licence will not be required to manufacture Class 1 biologicals. In order to obtain a manufacturing licence, a manufacturer must show that it complies with the manufacturing principles which will be an agreed Australian/New Zealand Code of GMP for human blood and tissues.

Under the joint regulatory scheme, it will be unlawful to manufacture a biological in Australia or New Zealand unless it is the subject of a product approval issued by ANZTPA, or it is otherwise exempted, approved or authorised.

## Obtaining a manufacturing licence

To obtain a manufacturing licence, the manufacturer will need to submit an application to ANZTPA. The application will need to:

- identify the biologicals that the applicant proposes to manufacture
- identify the premises where the biologicals will be manufactured
- identify the steps in manufacture that the applicant proposes to carry out
- state the names, qualifications and experience of the people who will control the production of the products and specify the quality control measures that are to be employed.

ANZTPA will be able to obtain additional information from the applicant and may require the applicant to allow an authorised person to inspect the premises, equipment, processes and facilities that will be used in the manufacture.

A manufacturing licence will be granted if ANZTPA is satisfied that:

- the applicant will be able to comply with the manufacturing principles
- the premises are satisfactory for the manufacture of the products
- the applicant and anyone else with significant involvement in the manufacture is a 'fit and proper person'.

A manufacturing licence will relate to a particular manufacturer and manufacturing site, specified step(s) in manufacture and specified type(s) of product.

## Conditions on a manufacturing licence

ANZTPA will be able to impose conditions on a manufacturing licence. A manufacturing licence will be granted subject to standard conditions including the following**.**

- ensure that the biologicals conform to any applicable standards
- ensure that the manufacturing principles are observed in carrying out any steps in the manufacture of biologicals under the licence
- keep appropriate records relating to the manufacture of the biological and retain these records for at least 12 months after the expiry date of the product to which they relate
- allow an authorised person to enter the manufacturing premises, to inspect the premises, the products and any of the substances used in the manufacture; take samples or copy documents.

In addition to the standard conditions, ANZTPA will be able to impose special conditions on a manufacturing licence at the time it is granted, or subsequently, and may also vary or remove existing conditions.

## Suspension or revocation of a manufacturing licence

ANZTPA will be able to revoke a manufacturing licence or suspend a licence for a specified period of time if, for example, a condition of the licence is breached or the licence holder, or anyone else who has significant involvement in the manufacture, is not a fit and proper person.

In certain circumstances, ANZTPA would be able to revoke or suspend a licence without giving notice (for instance at the request of the holder or in exceptional circumstances). Otherwise ANZTPA will be required to give the licence holder an opportunity to make submissions in relation to any proposal to suspend or revoke the licence.

## Validity of a manufacturing licence

Consideration is being given to whether:

- once issued, a manufacturing licence will remain valid for a specified period (unless suspended or revoked during that time) to be reissued for a further specified period based on satisfactory compliance and inspection history; and
- the manufacturer should be required to make annual declarations that the details relating to the licence remain correct.

ANZTPA will be able to vary the terms of a manufacturing licence as a result of its consideration of a renewal application or as a consequence of an inspection. It will also have power to impose, vary or remove conditions on the licence at any time.

## Exemption from manufacturing licensing

Class 1 biologicals will be exempt from the requirement to be manufactured by a licensed person. Additionally, certain persons will be exempt from the requirement to obtain a manufacturing licence when manufacturing specified biologicals in specified circumstances but subject to any applicable conditions.

## Overseas manufacturers

If a step in the manufacture of a biological has been carried out at a place outside Australia and New Zealand, ANZTPA must be satisfied that the manufacturing and quality control procedures used in each such step are acceptable.

As for medicines, a person seeking the product approval must supply evidence to ANZTPA that each manufacturer involved has acceptable manufacturing and quality control procedures in place. ANZTPA will consider whether the overseas manufacturer complies with the manufacturing principles and if satisfied will issue a document indicating that the particular manufacturer has the clearance to perform those steps in manufacture specified in the document. The clearance will be granted for a specified period.

ANZTPA will reserve the right to undertake an inspection of an overseas manufacturing site, irrespective of any other evidence supplied. An inspection could take place prior to initial clearance being given or at any time after.

# PRODUCT APPROVALS

For Class 1 biologicals an applicant must submit a statement of compliance with the mandatory standards. ANZTPA will review the statement of compliance but will not further evaluate the product before an approval is granted. As noted above, manufacturers of Class 1 biologicals will not need a manufacturing licence.

An application to supply a Class 2 biological will need to include a dossier demonstrating compliance with relevant standards. This dossier will be evaluated by ANZTPA before any approval is given. Manufacturers will also be required to show that they comply with the manufacturing principles; this could be demonstrated by a current ANZTPA manufacturing licence.

Before a Class 3 biological can be supplied it must be evaluated by ANZTPA for safety, quality and efficacy. This evaluation will be based on information supplied in a product dossier which should include sections on nonclinical and clinical development. Manufacturers must also show that they comply with the manufacturing principles.

An application for approval to supply a Class 4 biological will require submission of supporting data, and must be evaluated by ANZTPA for safety, efficacy and quality (as for Class 3). The level of detail required to be included in the dossier will correspond to the potential risk that the product poses to the recipient. Manufacturers must also show that they comply with the manufacturing principles.

Approvals for biologicals will be treated in the same way as for other therapeutic products, that is, they may be subject to conditions, may be varied and may be suspended or revoked.

# Obtaining Information

Effective regulation depends on the timely availability of relevant and accurate information. ANZTPA will be able to require product approval holders or licensed manufacturers (as well as applicants for approvals and licences) to provide information about therapeutic products or the manufacture of therapeutic products. Penalties will apply if the information is not provided in a timely manner or is false or misleading.

Failure to provide the information in relation to an approved product may also result in regulatory action such as the suspension or cancellation of an approval. ANZTPA will also be able to require former approval holders and former licensed manufacturers, as well as those lawfully supplying products that are exempt from approvals or licences, to provide relevant information.

# Exemptions from Product Approvals

The joint regulatory scheme will provide access to unapproved therapeutic products including, but not limited to, therapeutic products:

- for the treatment of a specified person or by an authorised medical practitioner, including when used in life-threatening circumstances
- imported for use in the treatment of the importer or the importer's immediate family
- "custom-made" in accordance with a request by a health professional and intended to be used for a particular individual, or dispensed or extemporaneously compounded for a particular person for therapeutic application
- to be used in emergency situations or to be stockpiled in preparation for dealing with a potential threat to public health caused by an emergency
- that could act as a substitute for an approved product that is temporarily unavailable or in short supply.

The joint regulatory scheme will also enable unapproved therapeutic products to be used in clinical trials. All clinical trials conducted in New Zealand or Australia will be required to meet relevant ethical standards as well as international standards for Good Clinical Practice. In order to balance the need to protect trial participants with providing a regulatory environment that can foster clinical research, consideration is being given to providing two avenues for allowing access to therapeutic products for use in clinical trials:

- a review process for trials involving products that are likely to pose a high risk to participants (for example high risk products being used for the first time in humans); and
- a certification process for all other trials.

# Post Market Monitoring and Compliance

Generally speaking, all activities undertaken by the regulator prior to approval of a product for market entry are described as pre-market regulatory activities, while all activities performed once the product has been supplied into the marketplace are described as post-market regulatory activities. Even so, it should be recognised that therapeutic products have a "life cycle," starting with research and development, through to regulatory approval, and finally, use in the "real world."

No therapeutic product is completely risk-free. Over time and as a therapeutic product's use becomes more widespread, more information becomes available that will lead to a better understanding of the risks and benefits associated with the product. Once in the market place, the additional information will be available to ANZTPA through a process of continuous monitoring that can inform regulatory actions taken to protect the public health.

As part of this continuous monitoring, approval holders may be required to provide ANZTPA with information regarding their products, this information may include distribution data.

## Spontaneous adverse event reporting

ANZTPA will have systems, procedures and strategies in place for the reporting of problems with all therapeutic products. ANZTPA will be responsible for a comprehensive adverse event reporting program monitoring the safety of therapeutic products supplied in Australia and New Zealand.

Manufacturers and approval holders will be required, by means of offence provisions in the legislation and conditions on approvals to actively monitor the performance of their products in the market place and will be required to report adverse events involving their products to ANZTPA within statutory timeframes that depend on the seriousness of the event. ANZTPA will review adverse event reports and undertake investigations if required. The nature of the information to be reported to ANZTPA will depend on the nature of the product and the seriousness of the event. It will be an offence if a product approval holder fails to provide the required information within the specified period and a ground to take other regulatory action against the approval holder.

Other features of the adverse event monitoring program will include international information exchange between regulatory authorities and between inter-governmental agencies within Australia and New Zealand and ANZTPA making available information to the public on adverse events and an "early warning" systems to communicate potential safety issues with therapeutic products.

Whilst it will be mandatory for approval holders and manufacturers to report adverse events associated with their products, health care professionals and consumers will also

be able to report any suspected problems with therapeutic products to ANZTPA and will be encouraged to do so.

ANZTPA will have systems for the dissemination of information to healthcare professionals and consumers on problems identified with therapeutic products.

# Risk management

The collection and monitoring of spontaneous adverse event reports is the cornerstone of any post-market vigilance program. However, although important, spontaneous adverse event reporting cannot answer all of the questions regarding the safety of a product in the post-market environment.

In order to assist early market entry for therapeutic products and to ensure ongoing safety of products in the market, ANZTPA will implement systems for managing the known risks of therapeutic products in the post-market environment. These systems will include risk management strategies to enable early detection and communication of risks whilst the products are in the marketplace and may include the requirement for formally agreed risk management plans for higher risk products. These formal risk management plans may require product approval holders to undertake specific, mandatory vigilance activities.

ANZTPA will be able to impose post-market requirements on the approval holder at any time in the product's life-cycle, not just at the time of approval. If, following approval, it becomes apparent that there are issues with the product, either from a safety or a performance perspective, ANZTPA will be able to impose requirements (including through the imposition of additional approval conditions) designed to manage the risks of the product or alternatively ANZTPA could remove the product from the market (including through a recall).

In assessing and approving risk management/vigilance plans ANZTPA will require sufficient knowledge of the pre-clinical and clinical safety of the product in order to make a valid assessment of the suitability of a proposed risk management/vigilance plan.

Failure of approval holders to meet post-market requirements may result in regulatory action, both in relation to the product itself (such as removal from the market or the imposition of additional conditions) or enforcement action against the approval holder (for instance in the event that there has been a breach of its obligations under the legislation to report adverse events).

# Surveillance and testing

Post market surveillance of therapeutic products by ANZTPA will include the compliance testing of products and the ability to audit documents and certifications for products not assessed as part of an application to supply the product in Australia or New Zealand.

ANZTPA's testing programs for medicines, medical devices and biologicals will assist with the investigation of adverse reaction reports, adverse incident reports and complaints in relation to therapeutic products and will also be used for post-market testing of therapeutic products for compliance with relevant standards and other requirements.

ANZTPA will be able to obtain samples of therapeutic products for testing and will have in place systems to ensure the integrity of its testing programs.

ANZTPA's powers will extend to therapeutic products that are being supplied unlawfully.

# Recalls and public notification

When a possible safety hazard or defect has been identified in a therapeutic product, it is vital that suppliers have efficient recall procedures in place to stop the distribution of the affected product and to remove any product that is potentially unsafe from the market. Without effective recall procedures in place, ANZTPA will not be able to assure the quality, safety and effectiveness/performance of therapeutic products available in Australia and New Zealand.

The following conditions will lead to consideration of the need for a recall action in relation to a therapeutic product in the marketplace:

- non-conformity with applicable standards
- non-compliance with manufacturing principles
- the quality, safety or efficacy/performance of the product is unacceptable
- the product's approval has been suspended or revoked
- in the case of a medical device, it does not comply with the essential principles, the conformity assessment procedures have not been applied or the device is not fit for its intended purpose
- the product is neither approved for supply nor exempt from the requirement to be approved
- the product is counterfeit or it has been or could be the subject of tampering.

In most cases, a recall would be considered necessary for reasons related to quality, safety or efficacy/performance of the product.

The recall of a therapeutic product could be initiated voluntarily by a product approval holder or ordered by ANZTPA. When the need for a recall has been established, the product approval holder for the affected goods will be required to assume the responsibility for recovery of the goods, or other corrective action. A recall may be requested by ANZTPA following identification of a potential safety issue, or following enforcement or compliance action. In these circumstances the recall will be negotiated with, and agreed to by, the product approval holder.

If necessary, ANZTPA will be able to order the approval holder to conduct a compulsory recall in the circumstances described above to protect the public from an unsafe good. When this happens, ANZTPA will direct the manner in which the recall is to occur and will enforce compliance. ANZTPA would usually only order a recall when the product poses a safety risk and the supplier is not prepared to recall the products voluntarily.

ANZTPA will set out procedures to be followed when recalling therapeutic products. It will be an offence for a person to fail to comply with a requirement imposed by ANZTPA to recover therapeutic products.

Where the circumstances that would warrant a mandatory recall have occurred then, in addition to the power to require a person to recall products from the supply chain, ANZTPA may require the same person to inform the public (or a specified class of persons) what is happening or has happened in relation to the product, and why; or publish specified information relating to the manufacture or distribution of the product. These requirements will extend to therapeutic products that are in the market place but are no longer being supplied.

## Seizure of therapeutic products

ANZTPA will have no authority to compel anyone other than the approval holder (or supplier if the product was not approved or is no longer the subject of an approval) or manufacturer to recall therapeutic products; however ANZTPA will have the power to seize therapeutic goods from any premises in particular circumstances including where seizure is in the interests of public health.

# Promotion of Therapeutic Products

Advertisements for therapeutic products will be required to meet specified requirements to ensure that they:

- are truthful and are not misleading
- do not promote inappropriate or unsafe use of the product.

In addition, it will be unlawful to advertise an unapproved therapeutic product, or to advertise an approved product in a manner that is inconsistent with the terms of its approval (for example, by advertising a medicine for an unapproved indication).

The content requirements for advertisements will vary depending on the type of advertisement and the type of product being advertised and will be set out in the legislation and an advertising code issued by ANZTPA.

There would be future consultation as part of the development of the advertising requirements.

# Provision of Expert Advice

ANZTPA will be able to establish expert advisory committees to advise on matters relating to its regulatory functions. Matters on which ANZTPA may seek expert advice will include, but will not be limited to, standards to be applied to therapeutic products, aspects of the

safety and efficacy or performance of particular therapeutic products in both pre and post market, and in relation to the advertising of therapeutic products.

# Fees & Charges

ANZTPA will be funded on the basis of full cost recovery. All activities undertaken by ANZTPA as part of pre-market, post-market monitoring and compliance and general enforcement activities in relation to therapeutic products regulated under the scheme will be funded by the collection of fees and charges.

To achieve full cost recovery, a range of fees and charges would apply. For example, fees would apply to the consideration of the approval of products and of the licensing of manufacturers; the level of these fees would be based on the cost of providing that service. Annual charges will be levied on approval and licence holders and these charges will be set at a level to cover ANZTPA's costs in maintaining its post-market monitoring and compliance functions and enforcement activities.

# Review of Decisions

There will be the ability for an applicant or person affected by a decision of ANZTPA to seek a review of the decision. In the first instance a review may be conducted internally by the Agency, but there will be provision for external merits review to an administrative tribunal whose members are to be drawn from a panel of persons appointed by the Ministerial Council.

Judicial review of decisions will be available in both countries consistent with the legal framework in place in each and the implementing legislation.