REGULATION OF IN VITRO DIAGNOSTIC TESTS IN AUSTRALIA

Report by the National Cancer Control Initiative

June 2001
Comment

The following report and summary reflects the current understanding of the National Cancer Control Initiative (NCCI) in regard to the marketing of in vitro diagnostic tests in Australia. This issue involves the review and interpretation of complex legal documents. The report and summary should not be taken to represent an authoritative opinion on the matter and do not represent a legal interpretation.

Recent concerns have arisen with the direct marketing to the public of screening tests for colorectal cancer that use faecal occult blood detection systems. While faecal occult blood screening in the context of a fully coordinated systematic screening program has been shown in randomised trials to be beneficial, questions have been raised about the direct marketing to the public of such tests. This is both in view of the possible lack of coordination with the necessary information and follow-up processes and because the tests being marketed may not be the same tests as those evaluated in large-scale studies.

In Australia, control for the supply of therapeutic products is provided by the *Therapeutic Goods Act*. Therapeutic products that are directly marketed to the public are also subject to the *Therapeutic Goods Advertising Code*. In this report we have reviewed the current control for in vitro diagnostics, which is the category covering faecal occult blood tests (FOBT).

**Regulation of Faecal Occult Blood Tests – Summary**

**Background**

Under the *Therapeutic Goods Act*, unless specifically excluded or exempted, therapeutic products must be entered in the *Australian Register of Therapeutic Goods* (ARTG) before they can be legally supplied to the Australian market. Entry of products into the ARTG is achieved by submitting an application to the *Therapeutic Goods Administration* (TGA). The TGA assesses the application and if the application is successful grants approval for marketing.

Not all therapeutic products have to undergo this approval process. As indicated above, under the *Therapeutic Goods Act* certain products are exempted from the requirement to be entered into the ARTG. Although these products do not have to be approved by the TGA, they must still comply with labelling and advertising provisions of the *Therapeutic Goods Act*. For some products specific conditions are also attached.

Therapeutic products are entered into the ARTG at one of two levels, ‘registered’ or ‘listed’. Registrable products are considered to have a higher level of risk and have to undergo an extensive pre-market evaluation by the TGA prior to approval for supply in Australia. Registered products are evaluated for quality, safety and efficacy. Listed products do not have
to undergo the same degree of evaluation. Products in the listed category are evaluated for quality and safety. It is our understanding that ‘quality’ in this context relates to quality of manufacturing.

Listing a device in the ARTG does require the sponsor to make a number of declarations in relation to the product that are based on the sponsor having documentary evidence on file to substantiate those declarations. The TGA does not examine this evidence at the time of listing but can do so later.

**Faecal Occult Blood Tests**

Under the *Therapeutic Goods Act*, it appears that FOBTs are defined as a ‘therapeutic device’ and are classified as an ‘in-vitro diagnostic’ (IVD). The current situation appears to be that IVDs that are for professional or laboratory use, apart from those that contain products of human origin, are supplied as a Pharmaceutical Benefit or are used to test for HIV or Hepatitis C infection, can be supplied in Australia without being registered or listed in the ARTG. FOBTs being used by a pathology laboratory may therefore be exempt from entry in the register and thus not have to be approved by the TGA.

IVDs that require being registered in the ARTG include those for testing for HIV or Hepatitis C infection. IVDs that require listing include those supplied as a Pharmaceutical Benefit, those containing material of human origin such as sera and those intended for home use. It is our understanding that IVDs considered to be ‘home use’ include those where the sample is collected and supplied by the individual seeking testing, the reading and interpretation of the test is performed in a laboratory and the result returned to the individual from whom the sample was taken. In the situation where there is an FOBT designed for use as described above, such a test may fall into the classification of ‘home use’ and thus require listing in the ARTG.

All listable FOBTs that are for home use or are supplied as a Pharmaceutical Benefit must have adequate instructions and information in plain English that clearly outlines the nature, use and limitations of the test.

**Advertising**

The *Therapeutic Goods Advertising Code* sets standards for advertising of therapeutic goods and would seem to be applicable to the situation of FOBTs being directly sold to the public. Advertisements for therapeutic devices (which include FOBTs) do not require formal approval. There are restrictions on advertising therapeutic goods for serious forms of certain diseases including serious forms of gastrointestinal disease. In this instance referral to the disease can only be made if prior approval has been obtained from the TGA. How this relates to the advertising of FOBTs is unclear.

It appears that therapeutic claims made to promote products that are listed in the ARTG and supplied directly to the public are assessed for compliance with the *Therapeutic Goods Advertising Code*. Evidence to substantiate product claims does not have to be presented in the application for listing, however, it is a condition of listing that this evidence be produced upon request.
**Proposed Changes to the Regulation of IVDs**

Modifications to the *Therapeutic Goods Act* are currently under consideration. Changes to the system are designed to harmonise the regulation of medical devices in Australia with those internationally. At this time, the proposed changes to the *Therapeutic Goods Act* do not include changes to the regulation of IVDs. The TGA has announced that it is to continue to consult on the inclusion of IVDs in the new regulatory system. For the time being IVDs will continue to be regulated as at present.

Among the proposed changes to the regulation of IVDs are that all IVDs would be required to be entered in the ARTG. This would result in a higher level of regulation for some tests currently supplied in Australia.

Two alternative approaches to classifying IVDs are currently being considered, the European approach and the Canadian approach. The Canadian approach divides therapeutic goods into four classes, with classes representing various levels of health risk. In the Canadian approach, cancer screening tests are specifically mentioned as being in class three, with class four being the highest risk. The European approach does not specifically mention cancer screening, but has similar general categorisation into risk type.

Of overseas systems to which the Australian situation is currently being compared, it would appear that FOBTs would be covered in the second highest risk category under the Canadian approach, and may be classified similarly under the European scheme.
Regulation of In Vitro Diagnostic Tests in Australia

National Cancer Control Initiative
2001
This document addresses the issue of how in vitro diagnostic tests are regulated in Australia. It has been complied by the National Cancer Control Initiative (NCCI). Information contained in this document was obtained from the Australian Medical Device Requirements Version 4, TGA Conformity Assessment Branch, Commonwealth of Australia, Canberra 1998, and the Internet websites of the Australian Therapeutic Goods Administration and the Australian Therapeutic Goods Advertising Code Council (last accessed 15 June 2001).


ACKNOWLEDGMENTS

The NCCI would like to thank Shelley Tang from the Conformity Assessment Branch of the Therapeutic Goods Administration for assistance with the preparation of this report.
IMPORTANT NOTICE

This document describes the regulation of in vitro diagnostic tests in Australia. While every effort has been made to ensure that the information given is correct and current, some information in this document may be subject to change due to amendments to Australian legislation and changes within the Therapeutic Goods Administration. This report represents the understanding of the NCCI with respect to the current regulation of in vitro diagnostic tests in Australia. The NCCI can not guarantee and assumes no legal responsibility for the accuracy of the information contained in this document.
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EXECUTIVE SUMMARY

In Australia the supply of therapeutic goods (products for which therapeutic claims are made) to the Australian market is regulated by the *Therapeutic Goods Act 1989*. The Act aims to ensure the quality, safety and efficacy of therapeutic products available in Australia. Unless a product is specifically excluded or exempted under the Act, there is a requirement that it be entered into the Australian Register of Therapeutic Goods (ARTG) before it can be legally supplied in this country. The ARTG is a database containing the details of therapeutic goods that are approved for supply in, or export from, Australia. Products for which entry in the ARTG is required are defined in the Regulations to the Act (*Therapeutic Goods Regulations*) and Orders made under the Act (*Therapeutic Goods Orders*). Information about products entered in the ARTG may be obtained upon request, although some information held is classified as confidential and is not available for release.

Therapeutic goods are divided into two classes – drugs and devices. To enter a product in the ARTG, the sponsor of the product (the company or individual that manufacturers, imports or modifies the product for the Australian market) submits an application to the Therapeutics Goods Administration (TGA). The TGA is a division of the Federal Department of Health and Aged Care. It is the body responsible for administering the *Therapeutic Goods Act* and maintains the ARTG. The TGA undertakes a variety of activities relating to the regulation of therapeutic goods in Australia, including premarket assessment, licensing of manufacturers and post-market monitoring. The branch of the TGA that is responsible for regulating therapeutic devices is the Conformity Assessment Branch.

Therapeutic goods that are not specifically excluded from the operations of the *Therapeutic Goods Act* (excluded goods) are regulated in three categories – registrable, listable and exempt. Products categorised as ‘registrable’ undergo a more rigorous evaluation prior to entry in the ARTG than products categorised as ‘listable’. Registrable products are evaluated for quality, safety and efficacy, while listable products are evaluated for quality and safety. Products that are categorised as exempt do not need to be entered in the ARTG before they can be supplied in Australia. Although they are exempted from inclusion in the ARTG, these products must still comply with advertising and labelling requirements of the *Therapeutic Goods Act* and other relevant Standards.

In vitro diagnostics (IVDs) are products that are intended by the manufacturer to be used in vitro for examining specimens to provide information about a person’s state of health or disease. In Australia IVDs are classified as therapeutic devices. Currently, only a limited number of in vitro diagnostic tests are required to be entered in the ARTG. These are:

- in vitro tests for diagnosis of HIV or Hepatitis C infection (registrable)
- in vitro tests that are for home use (listable)
- in vitro tests which are supplied as a Commonwealth Pharmaceutical Benefit (listable)
- tests that contain material of human origin, including sera and controls (listable)

All other IVDs can be supplied in Australia without being entered into the ARTG. This includes IVDs that are for professional / laboratory use and which do not contain products of human origin. Such products, however, must still comply with advertising and labelling requirements and other relevant Standards.
In Australia, healthcare products available without prescription from pharmacies, health food stores, supermarkets and by direct marketing can be advertised to the public. All advertisements and generic information provided about therapeutic goods directed to the public must comply with the *Therapeutic Goods Advertising Code* (TGAC). The object of the Code is to ensure that the marketing and advertising of therapeutic products to consumers is conducted in a manner that promotes the appropriate use of the product, is socially responsible and does not mislead or deceive the consumer. Advertisements for therapeutic goods directed exclusively to healthcare professionals are governed by industry codes of practice and are not subject to the TGAC.

The Therapeutic Goods Advertising Code Council (TGACC) considers the requirements for advertising therapeutic goods and makes recommendations to the Minister for Health and Aged Care. Members of the Council include the Australian Association of National Advertisers, the Complementary Healthcare Council, The Pharmacy Guild of Australia, the Royal Australian College of General Practitioners and the TGA. Advertisements for therapeutic devices do not require formal approval. They must, however, comply with the *Therapeutic Goods Act*, *Therapeutic Goods Regulations* and the TGAC.

The regulatory process for therapeutic devices is currently under review. The TGA is in the process of implementing an internationally harmonised regulatory system for medical devices. With respect to the regulation of IVDs, it is proposed that Australia adopt a similar approach to the European Union. This would result in a higher level of regulation for many IVDs supplied in this country. Two options are being considered for the classification system for IVDs in Australia – one based on the European system, the other on the Canadian approach.

It is anticipated that the new harmonised regulatory system for medical devices will be implemented in late 2001. Changes currently being made to the legislation do not at this time include changes to the regulation of IVDs. The TGA is to continue consulting on the inclusion of IVDs in the new regulatory system. For the time being IVDs will continue to be regulated in Australia as at present.
REGULATION OF THERAPEUTIC GOODS IN AUSTRALIA – AN OVERVIEW

What is a Therapeutic Good?

Essentially, a therapeutic good is a product for which a therapeutic claim is made. In defining what is a therapeutic good, the Therapeutic Goods Administration (TGA) states that:

‘A ‘therapeutic good’ is broadly defined as a good which is represented in any way to be, or is likely to be taken to be, for therapeutic use, unless specifically excluded or included under Section 7 of the Therapeutic Goods Act 1989.

For the purposes of evaluation and assessment, a therapeutic good is a product for use in humans that is used in, or in connection with:

- preventing, diagnosing, curing or alleviating a disease, aliment, defect or injury;
- influencing inhibiting or modifying a physiological process;
- testing the susceptibility of persons to a disease or ailment;
- influencing, controlling or preventing conception;
- testing for pregnancy; or
- replacement or modification of parts of the anatomy.’

Source: TGA website

Drugs and Devices

Therapeutic goods are divided broadly into two classes – drugs and devices.

Drugs are defined as:
Therapeutic goods that are represented to achieve, or are likely to achieve, their principal intended action via by pharmacological, immunological or metabolic means in or on the body of a person or animal; and any other therapeutic goods declared by the Secretary, by a notice published in the Gazette1, not to be therapeutic devices.

Therapeutic devices are defined as:
Therapeutic goods consisting of an instrument, apparatus, material or other article (whether used alone or in combination), together with any accessories or software required for their proper functioning, which do not achieve their principal intended action by pharmacological, chemical, immunological or metabolic means though it may be assisted in its function by such means, but does not include therapeutic goods declared by the Secretary, by order in the Gazette1, not to be therapeutic devices.

Source: TGA website

In vitro diagnostic tests (in vitro diagnostics; IVDs) are classified as therapeutic devices.

1 Therapeutic Goods Order No 1 of 1992 – Goods that are not Therapeutic Devices
The Therapeutic Goods Act

In Australia, the supply of therapeutic goods is regulated by the *Therapeutic Goods Act 1989* (the Act). The Act, which came into effect on 15 February 1991, provides a legislative basis for uniform national controls over goods used in the prevention, diagnosis, curing, or alleviation of a disease, ailment, defect or injury. The *Therapeutic Goods Act* aims to ensure the quality, safety and efficacy of therapeutic products available in this country.

Australian Register of Therapeutic Goods

Unless specifically excluded or exempted under the Act, products for which therapeutic claims are made must be entered in the Australian Register of Therapeutic Goods (ARTG) before they can be legally supplied to the Australian market.

The ARTG is a computer database containing information about therapeutic goods for human use that are approved for supply in, or export from, Australia. Information held on the database includes:

- Product name and formulation details
- Sponsor and manufacturer details

Currently the ARTG holds information on approximately 25,000 drug and 24,000 therapeutic device products. Products for which entry in the ARTG is required are defined in the regulations to the Act (*Therapeutic Goods Regulations*) and Orders made under the Act (*Therapeutic Goods Orders;* TGO’s). These Regulations and Orders also define products that are excluded or exempted from the requirement to be entered in the ARTG.

Information on products entered in the ARTG is available upon request (Regulation 46 of the *Therapeutic Goods Regulations*). Some information held on the register is classified as confidential and is not available for release. Release of information may also incur charges.
THE THERAPEUTIC GOODS ADMINISTRATION

The TGA is a division of the Federal Department of Health and Aged Care. It is the body responsible for administering the Therapeutic Goods Act and carries out a range of activities, including assessment and monitoring, to ensure that therapeutic goods available in Australia are of an acceptable standard. The TGA is comprised of a number of branches. These are shown in Figure 1.

BSB = Business and Services Branch
CNPMB = Chemical and Non Prescription Medicine Branch
CAB = Conformity Assessment Branch
DSEB = Drug Safety and Evaluation Branch
TGAL = TGA Laboratories Branch


The TGA controls the supply of therapeutic products through three main processes:

- Premarket assessment
- Licensing of manufacturers
- Post-market vigilance

Premarket Assessment

Evaluation of therapeutic goods for entry in the ARTG is undertaken by the TGA with advice from expert committees, as required. Assessment of therapeutic devices is undertaken by the Conformity Assessment Branch (CAB) with advice, if required, from the Therapeutic Devices Evaluation Committee (TDEC). Contact details and a list of committee members for the TDEC is available from the TGA website at http://www.health.gov.au/tga/docs/html/tdec.htm
Products assessed as having a higher level of risk, such as prescription medicines and high-risk medical devices, are evaluated for quality, safety and efficacy. Once approved for marketing in Australia these products are included in the ARTG as ‘registered’ products and are identified by an \textit{AUST R} number.

Products assessed as being of lower risk, including low-risk medical devices, are assessed for quality and safety. Once approved for marketing in Australia, these products are included in the ARTG as ‘listed’ products and are identified by an \textit{AUST L} number.

When assessing the level of risk of a product, the TGA takes into account various factors including:

- The strength of the product
- Side effects
- Potential harm through prolonged use
- Toxicity
- The seriousness of the medical condition for which the product is intended to be used

**Licensing of Manufacturers**

Australian manufacturers of therapeutic goods must be licensed and their manufacturing processes must comply with the principles of good manufacturing practice (GMP). Licensing standards for therapeutic products aim to protect public health by ensuring that the products produced meet definable standards for quality assurance and are manufactured in conditions that are clean and free of contaminants.

**Post-marketing Vigilance**

Post-marketing activities conducted by the TGA include:

- Investigating reports of problems with therapeutic goods
- Laboratory testing of products on the market
- Monitoring to ensure compliance with legislation

The TGA has in place an ‘Incident Reporting Scheme’ to monitor and investigate the causes and occurrences of incidents arising with therapeutic devices. Under this scheme the TGA collates and examines reports of suspected problems with therapeutic devices, which may present a health hazard, such as performance failures, poor design or deficiencies in labelling and instructions. Reports of problems can be supplied to the TGA either on a pre-printed ‘Medical Device Incident Report’ form or on plain paper. A copy of this form is available at the TGA website.

For therapeutic devices that are registered or listed in the ARTG, sponsors must inform the TGA of all deaths, serious illness or serious injury arising from or attributable in some way to the use or application of the device as soon as possible after they become aware of the incident.

For therapeutic devices that are required to conform with a \textit{Therapeutic Goods Order} or other Standard, the TGA may draw samples from sponsors at any time for evaluation and testing for compliance with the appropriate Standard. It is also a mandatory condition of listing or registration that for goods that are distributed overseas as well as in Australia, the sponsor must...
notify the TGA of any regulatory action taken in relation to the goods outside this country. This condition applies irrespective of whether the goods are manufactured in Australia or imported.

The TGA undertakes a number of post-market audit programs including checking distribution records and compliance with GMP (for selected goods). In addition, listing a therapeutic device in the ARTG requires sponsors to make a number of declarations relating to the goods, based on the sponsor having documentary evidence on file to substantiate those declarations. This evidence is not examined by the TGA at the time of listing, but can be reviewed at a later date.

CATEGORISATION OF THERAPEUTIC GOODS

Under the *Therapeutic Goods Act*, therapeutic products (both drugs and devices) are categorised as one of the following:

- Excluded
- Registrable
- Listable
- Exempt

Complete details of therapeutic goods and their classification according to the Act can be found in Schedules 3, 4 and 5 of the *Therapeutic Goods Regulations* and the *Excluded Goods Order*. These publications are available from Government Information Shops (see Appendix II).

**Excluded**

Some products, which may have a therapeutic use, are not regarded as therapeutic goods for the purposes of the Act. The *Therapeutic Goods (Excluded Goods) Order No 1 of 1992* provides a list of these types of products. If a product falls into this category, the *Therapeutic Goods Act 1989* does not apply and it does not have to be entered in the ARTG.

*Examples of excluded goods include:*
  - Unmedicated soaps and detergents
  - Dental whiteners and bleaches
  - Moisturisers, emollients, cleansers and barrier products, not for dispensing
  - Cosmetics without therapeutic claims
  - Spa and natural mineral waters with no therapeutic claims
  - Aids to physical comfort
  - Fitness equipment, excluding physiotherapy
  - Solaria and sun lamps
  - Sunglasses, nonprescription spectacles
  - Aromatherapy devices
  - Ostomy adhesive removers and nonmedicated cleansers
  - Menstrual pads, but not tampons

*Source: Australian Medical Device Requirements Version 4, DR4, pp 4.*

Products that are not excluded under the Act, are regulated in three categories with respect to the operation of part 3 of the Act (entry in the ARTG). These categories are registrable, listable and exempt.

**Registrable**

Products have to be ‘registered’ in the ARTG and have to undergo extensive premarket evaluation before they can be supplied in Australia. Therapeutic goods that must be registered are specified in Schedule 3 of the *Therapeutic Goods Regulations*. They are further sub-categorised into ‘high level registrable’ and ‘low level registrable’ goods. Sponsors of registrable products are required to submit data to establish the quality, safety and efficacy of their product for review by the TGA, prior to its inclusion in the ARTG.
Examples of registrable goods include:

- All Pharmaceutical Benefit drugs
- All other drugs unless listable or exempt
- Active implantable medical devices – eg implantable cardiac pacing systems, implantable pacing leads
- Breast implants
- Devices of human or animal origin
- Contraceptive barrier devices (where no standard is available)
- Disinfectants – hospital grade with specific claims, household/commercial grade with specific claims, instrument grade
- Heart valves
- HIV and Hepatitis C in vitro diagnostic kits
- Intraocular fluids
- Drug infusion systems – powered (except some simple pumps)
- Sterilants

Source: Australian Medical Device Requirements Version 4, DR4, pp 5.

Listable

Products have to be ‘listed’ in the ARTG but do not have to undergo extensive pre-market evaluation before supply. The sponsor has to provide the TGA with:

- Information that ‘reasonably demonstrates the safety and quality of the goods for the intended use’
- Test certificates and/or acceptable evidence of GMP, if required
- A label (either a sample or a draft) that complies with the Therapeutic Goods Order for labelling (TGO 37)
- Package inset/promotional material that complies with the Therapeutic Goods Advertising Code (TGAC)

In general, therapeutic claims made to promote a product supplied directly to the public will be assessed for compliance with advertising requirements (compliance with the TGAC). Evidence to substantiate such claims need not be presented in the application for product listing, however, it is a condition of listing that this evidence is to be produced on request. All therapeutic devices are subject to on-going post-market surveillance.

Examples of listable goods include:

- Sunscreens SPF4+ if correctly labelled; or SPF4 or less if containing human or animal tissue
- Medicated throat lozenges (volatile oils, vitamin C) with no unacceptable claims
- Bandages, dressings and allied products
- Blood bags and blood collection tubes
- Endoscopes and their accessories
- Condoms
- Contact lenses and contact lens care products
- Dental restorative materials
- Insulin syringes
Gloves examination/surgical
Tampons – menstrual
Sutures and ligatures
Hospital grade disinfectants for noncritical uses
Household/commercial grade disinfectants with nonspecific claims

Source: Australian Medical Device Requirements Version 4, DR4.

**Exempt**

Products are exempt from Part 3 of the Act (entry in the ARTG), but are still covered by labelling and advertising provisions of the Act. Therapeutic goods that are exempted from the requirement for entry in the ARTG are specified in Schedules 5 and 5A of the *Therapeutic Goods Regulations*.

*Examples of exempt goods include:*
  - Sunscreens below SPF4 if correctly labelled
  - Non-sterile, dilute (4X) homeopathics
  - Anti-dandruff products if unscheduled
  - Allergen patch tests
  - Containers (except syringes, solution bags and blood collection tubes)
  - Hot/cold packs
  - Orthoses or splints (simple)
  - Non-powdered, non-sterile diagnostic instruments
  - Manufacturing, laboratory and dispensary equipment not for recycling human blood or tissue
  - Goods for approved or notified clinical trials
  - Goods given special access for individual patients
  - Samples not for human use

*Note:* Exceptions and ‘fine print’ details can apply to exempt items. Advertising and labelling requirements apply to all exempt goods.

Source: Australian Medical Device Requirements Version 4, DR4, pp 5.
ENTRY INTO THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS

If a therapeutic device falls within the category requiring it to be registered or listed in the ARTG, the sponsor of the device (who must be an Australian entity) is responsible for seeing that it is entered into the register before it may be marketed. The sponsor is the company or individual that imports, manufactures or modifies the product for supply in Australia.

To enter a therapeutic device in the ARTG, the sponsor submits an application to the TGA. Information on applying for listing or registration of therapeutic devices is found in the ‘Australian Medical Device Requirement Version 4 under the Therapeutic Goods Act 1989 DR4’ and at the TGA Internet website. Application and annual charges apply for all registrable and listable devices. For registrable devices, evaluation fees also apply.

As part of the application process, sponsors complete and submit a Therapeutic Devices Application form. If the application is an initial one it must be accompanied by an Enterprise Details form, which contains sponsor details and nominates an authorised person. The sponsor is then allocated an Enterprise Identification Number (Enterprise ID code). Information provided to the TGA when applying for registration or listing of a product is confidential.

In completing a Therapeutic Devices Application form, a sponsor provides the TGA with the following information:

- Sponsor’s name and contact details
- TGA Enterprise ID code (if available)
- Contact details and signature of an authorised person
- A declaration that the information is current and correct
- Manufacturer(s) name, contact details and for Australian manufacturers their TGA licence number
- Export or import status
- Evidence of GMP certification (for overseas manufacturers)
- Evidence of compliance with prescribed quality and safety criteria (if applicable)
- Notification of any prior approval or refusal by other regulatory agencies
- Product name
- Brief description of the intended use and function of the product
- Source and type of material (if the product has been manufactured using material of human or animal origin)
- Sterility status
- For kit products, a list of therapeutic goods contained within the kit
- Description of container material and closure
Registrable Devices

Information that must be supplied to the TGA when applying for registration of a therapeutic device includes:

- A completed Therapeutic Devices Application form
- A completed Enterprise Details form (if applicable)
- Proprietary name of the device
- A brief description of the device
- Technical and clinical specifications for the device
- Labels (draft or sample)
- Packaging
- Product information / Instructions for use / Promotional material
- Any other media or material which could assist in the evaluation of the device

When applying for registration of the therapeutic device, for the purposes of evaluation a sponsor must ‘satisfactorily establish the quality, safety and efficacy’ of the product. In undertaking the evaluation, the CAB assesses the data provided to confirm that the device will operate in a safe and reliable way and that the specifications have been correctly implemented. The TGA may request a sample of the device for examination.

Assessment is achieved primarily through examination of the manufacturer’s own tests and through some in house testing. The review by the TGA may include assessing conformance to standards, assessment of testing protocols and results, and assessment of GMP and other regulatory requirements. In most cases, clinical or preclinical studies will be required to determine that the device specifications adequately match the operational requirements or clinical usage of the device.

The TGA evaluates the product and determines if the product is acceptable for registration and general marketing. If the product is acceptable a certificate of registration is issued and the sponsor may commence supply of the goods to consumers.


Listable Devices

When applying for listing of a therapeutic device the sponsor should submit:

- A completed Therapeutic Devices Application form
- A completed Enterprise Details form (if applicable)
- GMP evidence
- Test Certificates (where applicable)
- Labels (draft or sample)
- Product information – Promotional material / Instructions for use / Product insert
The TGA assess the information included in the application and determines if the product is acceptable for listing. If the product is acceptable a certificate of listing is issued and the sponsor may commence supply of the goods to consumers.

Categorisation of Goods under the *Therapeutic Goods Act 1989*

**Australian Register of Therapeutic Goods (ARTG)**
- ARTG entry required
  - (Part 3 Section 17)

**Registrable**
- (Schedule 3)
- GMP required

**Listable**
- (including goods for export only)
  - (Schedule 4)

- High level registrable
  - (Schedule 3 part 1)

- Low level registrable
  - (Schedule 3 part 2)

- Labelling & Advertising
  - GMP
    - (Schedule 6 or 7)
    - or Test Certificate

- Standard requirements: Labelling, Advertising

**Excluded Goods**
- (Section 7)
- declared not to be therapeutic goods

**Exemptions**
- from ARTG entry or GMP licensing

**Exempt Goods**
- Clinical Trials or Special Access Schemes
  - (Section 18 or 19)

**Exempt Goods**
- ARTG entry not required
  - (Section 18, Schedule 5)

- Advertising, Labelling & Standards apply

IN VITRO DIAGNOSTICS (IVDS)

The term ‘diagnostic goods for in vitro use’ includes:

- any medical device which is a reagent, reagent product, calibrator, control material kit, instrument, apparatus, equipment or system, whether used alone or in combination, that is intended by the manufacturer to be used in vitro for examining specimens including blood and tissue donation, taken from the body of a person. These devices are intended solely or principally for providing information about a person’s physiological state, state of health or disease, or congenital abnormality, or to determine the safety and compatibility of donor and recipient.

The term ‘in vitro diagnostics’ includes:

- any in vitro diagnostic device intended by the manufacturer to be used in the home environment for self testing, as well as those that are supplied under the Pharmaceutical Benefits Scheme for in vitro diagnosis.


The definition of ‘good for home use’ in relation to an IVD is:

- ‘goods supplied to a person for that person:
  (a) to use in diagnosing or monitoring a condition in that person or the immediate family of that person; or
  (b) to use in the collection of a sample of a body specimen of that person and, if the sample is tested by another person, if and only if, the results of the test are to be returned by that other person to the person from whom the sample was taken.’

Regulation of IVDs in Australia

Currently, the TGA regulates a limited number of IVDs as therapeutic devices. At present, only the following IVDs must be registered or listed in the ARTG before being supplied in Australia:

- IVDs for testing HIV and Hepatitis C virus infections (registrable)
- IVDs for home use (listable)
- IVDs supplied as a Pharmaceutical Benefit (listable)
- IVDs containing material of human origin, including sera and controls (listable)

All other IVDs can be supplied in Australia without being registered or listed (they are classified as exempt goods). This includes IVDs that are for professional/laboratory use which do not contain products of human origin and are not listed as a Pharmaceutical Benefit.
Specific conditions

For certain IVDs specific conditions must be complied with. These include the following:

- IVDs for home use and IVDs that contain material of human origin require evidence of GMP. IVDs containing material of human origin, must conform to the *Therapeutic Goods Order 34 – ‘Standard for Diagnostic Goods of Human Origin’*, a Test certificate must be provided upon request and the sponsor is required to keep detailed records of importation and distribution.

- HIV diagnostic tests may be supplied only to laboratories authorised by the relevant State or Territory health authority.

- IVDs for Hepatitis C virus that are registered as supplemental or which use new technology such as PCR or Branched DNA detection, may only be supplied to authorised laboratories.

- Listable IVDs for home use or that are supplied as a Commonwealth Pharmaceutical Benefit must:
  - be accompanied by adequate instructions and information in plain English and in Standard International Units, outlining clearly the nature, use and limitations of the test or equipment; and
  - be labelled with:
    - the name of the device
    - the name and address of the sponsor or manufacturer
    - the Batch or Lot number
    - the names and quality of all goods contained in the package

Australian manufacturers of IVDs must be licensed, and overseas manufacturers must provide acceptable evidence of GMP. The *Therapeutic Goods Act* requires that imported goods manufactured outside Australia comply with equivalent standards of manufacturing as expected for similar products manufactured in Australia.


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2 TGO 34 is a mandatory requirement. It specifies requirements for quality control of source material and testing for Hepatitis B and HIV. It also imposes additional labelling requirements. Supplying goods in Australia which do not comply with this Order is an offence under the Act. Goods not complying with TGO 34, will be subject to recall and sponsors may be prosecuted.
ADVERTISING THERAPEUTIC GOODS

In Australia, healthcare products available without prescription from pharmacies, health food stores, supermarkets and by direct marketing can be advertised to the public. All advertisements and generic information about therapeutic goods directed to the public must by law comply with the requirements and standards of the TGAC. The object of the Code is to ensure that the marketing and advertising of therapeutic products to consumers is conducted in a manner that promotes the appropriate use of the product, is socially responsible and does not mislead or deceive the consumer.


As defined in the *Therapeutic Goods Act 1989*, an ‘advertisement’ in relation to therapeutic goods includes any statement, pictorial representation or design that is intended to promote the use or supply of the goods. Advertisements for therapeutic devices do not require formal approval. They must, however, comply with the *Therapeutic Goods Act 1989*, *Therapeutic Goods Regulations* and the TGAC. All advertisements for therapeutic goods are subject to the *Therapeutic Goods Act and Regulations*, the Trade Practices Act and other relevant laws. Compliance with the TGAC does not exempt advertisements from the application of those laws.

The Therapeutic Goods Advertising Code

Regarding compliance with, and application of, the TGAC it is stated in the Code that:

- Advertisements for therapeutic goods directed to consumers must comply with the Code
- Advertisements for therapeutic goods directed exclusively to healthcare professionals are governed by industry codes of practice and are not subject to this Code
- This Code does not apply to bona fide news, public interest or entertainment

Principles

The following statements are included in the general principles listed in the TGAC.

An advertisement for therapeutic goods *must*:
- Comply with the statute and common law of the Commonwealth, States and Territories
- Contain correct and balanced statements only and claims which the sponsor has already verified

An advertisement for therapeutic goods *must not*:
- Be likely to arouse unwarranted and unrealistic expectations of product effectiveness
- Be likely to lead to consumers self-diagnosing or inappropriately treating potentially serious disease
- Mislead directly or by implication or through emphasis, comparisons, contrasts or omissions
- Abuse the trust or exploit the lack of knowledge of consumers or contain language which could bring about fear or distress
• Contain any matter which is likely to lead persons to believe that they are suffering from a serious ailment or that harmful consequences may result from the therapeutic good not being used
• Encourage inappropriate or excessive consumption
• Contain any claim, statement or implication that it is infallible, unfailing, magical, miraculous, a certain, guaranteed or sure cure
• Contain any claim, statement or implication that it is effective in all cases of a condition
• Contain any claim, statement or implication that the goods are safe or that their use cannot cause harm or that they have no side-effects

The general principles of the Code also contain directives relating to:
• Scientific information
• Comparative advertising
• Professional recommendation
• Testimonials
• Samples

Scientific information in an advertisement is to be presented in a manner that is accurate, balanced and not misleading. Scientific terminology must be appropriate, clearly communicated and able to be readily understood by the audience to whom it is directed. Publication of research results must identify the researcher and sponsor.

With respect to comparative advertising, comparative advertisements must be balanced and not misleading or likely to be misleading, either about the product advertised or that with which it is being compared. Comparisons should not imply that the product, to which it is compared, is harmful or ineffectual.

Prohibitions

Advertising therapeutic goods for serious forms of certain diseases, conditions or ailments are either prohibited or restricted. These prohibitions and restrictions are listed in Appendix 6 of the TGAC. References to the diseases in the Prohibited list cannot be made either expressly or by implication. References to diseases in the restricted list can only be made if prior approval has been obtained from the TGA.


Therapeutic Goods Advertising Code Council

The Therapeutic Goods Advertising Code Council (TGACC) is responsible for ensuring that the public interest is upheld for any advertisement of a therapeutic good. The TGACC considers the requirements for advertising therapeutic goods and makes recommendations to the Minister for Health and Aged Care.

Members of the TGACC include the:
• Australian Association of National Advertisers
• Australian Consumers Association
• Australian Direct Marketing Association
• Advertising Federation of Australia
• Australian Self-Medication Industry
A Complaints Resolution Panel (CRP) determines complaints arising about advertisements for therapeutic goods and generic information about therapeutic goods, including devices, that are broadcast on television, radio and in the cinema, published in newspapers or magazines or displayed outdoors, such as on billboards, bus sides or bus shelters.

If the CRP decides that an advertisement has breached the Code sanctions, including the withdrawal of the material from further publication or the publication of a retraction or correction, can be imposed on the company or person responsible. Failure to respond to such sanctions or a repetition of the claims in breach will result in the complaint being referred to the Australian Competition and Consumer Commission. In extreme cases, regulatory action may be taken to remove a product from sale.

Complaints regarding other advertisements, including those directed at healthcare professionals, are handled by different industry associations – namely the Complimentary Healthcare Council and the Australian Pharmaceutical Manufacturers Association.

PROPOSED CHANGES TO THE REGULATION OF IVDS

The regulatory process for therapeutic devices in Australia is currently under review. The TGA is in the process of implementing an internationally harmonised regulatory system for medical devices. The new system is to be in line with international best practice and will harmonise the regulation of medical devices with those of the European Union (EU) and the recommendations of the Global Harmonisation Task Force (GHTF)\(^1\). The new system will include a risk based classification system, minimum safety and performance requirements and harmonised quality assurance systems for manufacturing. With respect to the regulation of IVDs, it is proposed that Australia adopt a similar approach to the EU. This would result in a higher level of regulation for many IVDs supplied in this country.

The Therapeutic Goods Amendment (Medical Devices) Bill 2001 to allow the implementation of the new harmonised regulatory system for medical devices was introduced into Parliament in March 2001 and is due to be debated in the Winter 2001 sitting or Parliament. It is anticipated that the new harmonised system will be implemented in late 2001.

Changes currently being made to the legislation do not at this time include changes to the regulation of IVDs. The TGA is to continue to consult on the inclusion of IVDs in the new regulatory system. For the time being IVDs in Australia will continue to be regulated as at present.

Features of the Proposed Regulatory System

Key features of the proposed regulatory system for IVDs include:

- A risk based classification of IVDs
- Essential principles for safety and performance with which all IVDs must conform
- Conformity assessment procedures to ensure that IVDs meet the essential principles
- Demonstrated compliance with nominated international standards as a basis for presuming that an IVD conforms with the essential principles
- A post-market vigilance and surveillance system
- All IVDs to be entered on the ARTG

The conformity assessment process would require the manufacturer/sponsor to demonstrate that the product meets the Essential Principles for safety, quality and performance based on the manufacturer’s intended purpose. Performance evaluation would be a requirement for highest risk products, while for lowest risk products, the manufacturer/sponsor will self certify that the products meet the relevant Essential Principles.


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\(^1\) The GHTF is a voluntary international consortium of public health officials responsible for administering national medical device regulatory systems and representatives from the regulated industry. Its purpose includes encouraging convergence in regulatory practices related to ensuring the safety, effectiveness and quality of medical devices and serving as a forum for information exchange. Australia is one of the five members of the GHTF together with the USA, Canada, the European Union and Japan. Further information on the GHTF can be found at [http://www.ghtf.org](http://www.ghtf.org)
Alternative Classifications of IVDs

Two options are being considered for the classification system for IVDs in Australia – one aligning classification with the European system, the other aligning classification with the Canadian approach. A discussion paper was put forward presenting the two options and calling for comment. The period of comment closed in March 2000 and responses are now being considered. Further developments on the proposed changes are to be reported in *the Australian Therapeutic Device Bulletin* and notified at the TGA website. A decision on the classification system for IVDs in Australia has yet to be published.


A brief comparison of the two proposed classification systems is given below and in Table 1.

**European**
- Risk based classification
- Classification of high risk devices is by test type

**Canadian**
- Risk based classification
- Largely dependent on the information provided about a product’s intended use and the degree of risk associated with the use of an IVD
- IVDs classified into four classes (I – IV), with class I being the lowest risk category and class IV the highest risk category
Table 1. Comparison of the Proposed Classification Systems for In Vitro Diagnostics

<table>
<thead>
<tr>
<th>European Approach</th>
<th>Canadian Approach</th>
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</thead>
<tbody>
<tr>
<td>Annex II List A – includes test kits for HIV, HTLV and Hepatitis and some blood</td>
<td>Class IV – present a high public health risk, eg for donor screening, HIV, Hepatitis viruses.</td>
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<tr>
<td>grouping products including those used to test donated blood.</td>
<td>-------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>Annex II List B – includes (amongst others) test kits for anti-Duffy and anti-Kidd,</td>
<td>Class III – present a moderate public health risk or high individual risk, eg sexually transmitted</td>
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<tr>
<td>irregular anti-erythrocytic antibodies, cytomegalovirus, chlamydia, HLA tissue</td>
<td>diseases, cancer screening, meningitis, genetic testing, rubella, Adenovirus. All ‘near patient’ IVDs</td>
</tr>
<tr>
<td>groups, PSA, trisomy 21, rubella, toxoplasmosis and phenylketonuria, as well as</td>
<td>ie those for home-use or point of care testing.</td>
</tr>
<tr>
<td>self-test devices for blood glucose.</td>
<td>-------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Self-testing</td>
<td>Class II – present a low public health risk or a moderate individual risk, such a progesterone,</td>
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<td></td>
<td>glucose, cholesterol level, estradiol and tests for detection of pregnancy or fertility testing.</td>
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<tr>
<td>General</td>
<td>Class I – general in vitro diagnostic laboratory equipment, microbiology and cell culture media and</td>
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<tr>
<td></td>
<td>general diagnostic reagents. Microbiological media used to identify or infer the identity of a microorganism. IVD used to identify or infer the identity of a cultured microorganism.</td>
</tr>
</tbody>
</table>

APPENDIX I

CONTACT DETAILS

Therapeutic Goods Administration
General Inquiries
Mail: The Information Office
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606
Tel: 1800 020 653
TTY: 1800 500 236

Switchboard
Tel: (02) 6232 8444

Medical Devices
Conformity Assessment Branch
Tel: (02) 6232 8438

Publications
Publications Office
Tel: (02) 6232 8610

Therapeutic Devices Evaluation Committee
Secretary Rita Mclachlan
Tel: (02) 6232 8700

Executive Secretary Craig Davis
Tel: (02) 6232 8666
Fax: (02) 6232 8687

Postal Address: PO Box 100
WODEN ACT 2606
APPENDIX II

PUBLICATIONS REFERRED TO AND THEIR SOURCES

Copies of Legislation

The *Therapeutic Goods Act 1989*, and *Therapeutic Goods Regulations* and *Therapeutic Goods Orders* (TGO’s) may be obtained from Government Information Shops.

Government Info Shops
Tel: 132 447 in capital cities

TGA Publications Office

Copies of ‘Australian Medical Device Requirements DR4’, Therapeutic Device Application forms, TGO’s and current schedule of fees may be obtained by contacting the TGA Publications Office.

TGA Publications Office
Tel: (02) 6232 8610 or 1800 020 653
Fax: (02) 6232 8605
Email: tga-information-officer@health.gov.au

Copies of Standards

Copies of Australian and International Standards can only be obtained from Standards Australia.

Standards Australia
National Sales Centre
Tel: (02) 8206 6009
Email: sales@standards.com.au
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>ARTG</td>
<td>Australian Register of Therapeutic Goods</td>
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<tr>
<td>CAB</td>
<td>Conformity Assessment Branch</td>
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<tr>
<td>CRP</td>
<td>Complaints Resolution Panel</td>
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<tr>
<td>EU</td>
<td>European Union</td>
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<td>GHTF</td>
<td>Global Harmonisation Task Force</td>
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<td>Good Manufacturing Practice</td>
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<td>In Vitro Diagnostics</td>
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<td>Therapeutic Devices Evaluation Committee</td>
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REFERENCES


