
4 Therapeutic goods regulation

4.1 Overview of regulation

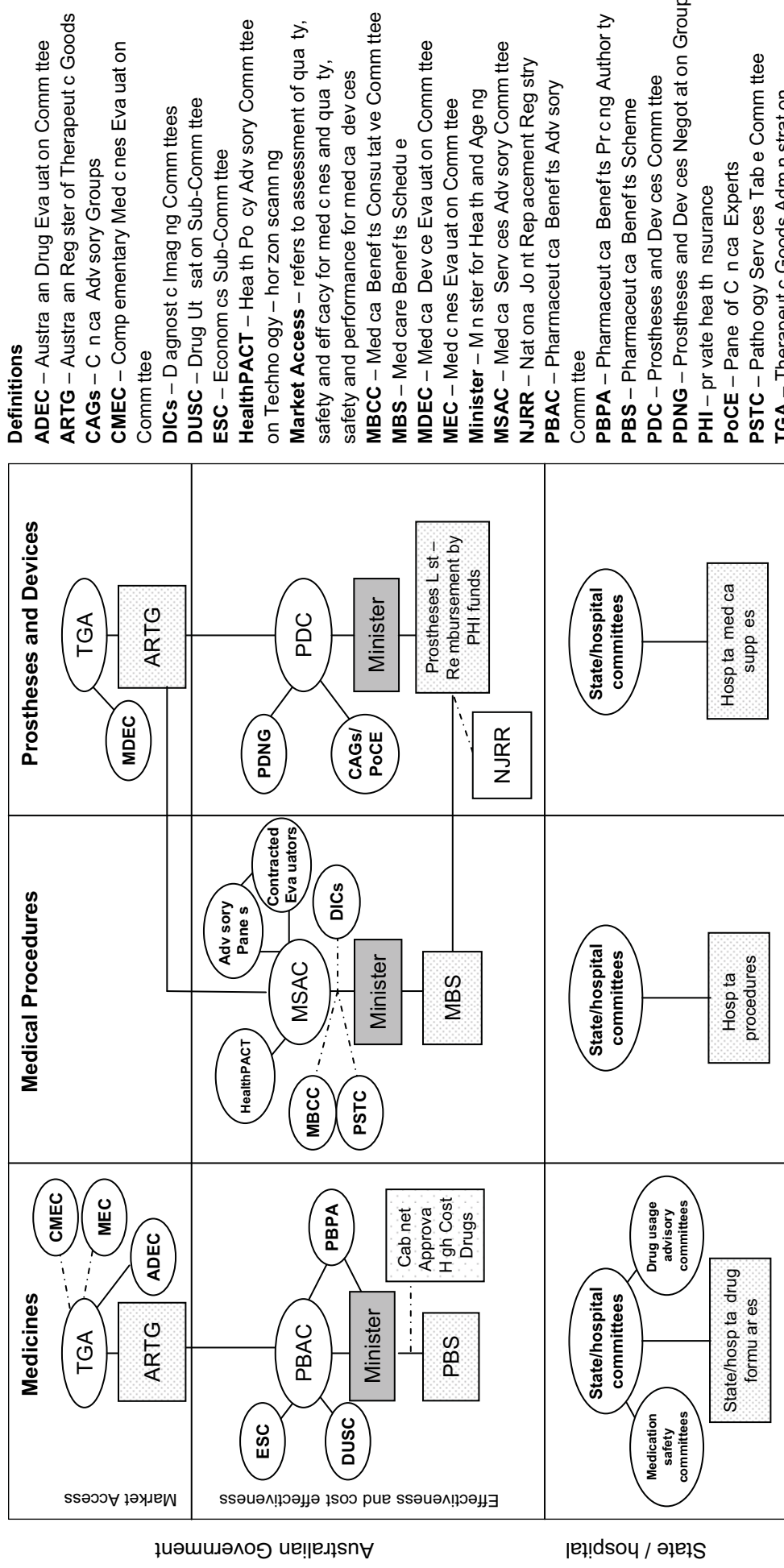
Regulatory control of the standard of therapeutic goods (medicines and medical devices) is provided by the *Therapeutic Goods Act 1989* (the Act) and associated regulations, orders and standards. The regulatory framework which applies nationally, with provisions adopted into state and territory legislation as relevant seeks to safeguard the community from substandard, unsafe or ineffective therapeutic goods.

Responsibility for the regulatory system, and administration of the Act and associated regulations and orders, lies with the Therapeutic Goods Administration (TGA), a unit within the Department of Health and Ageing (DOHA). Various other regulatory agencies and advisory bodies form part of the overall regulatory framework (see discussion below and figure 4.1). In the overview of the regulatory framework for medicines (below) and for medical devices in section 4.3, the Commission has described the roles of selected bodies only, focussing mainly on those considered most relevant to the specific concerns that have been raised.

A ‘therapeutic good’ is broadly defined in the Act as a good which is represented in any way to be, or is likely to be taken to be, for therapeutic use. Therapeutic use means use in or in connection with: preventing, diagnosing, curing or alleviating a disease, ailment, 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. A snapshot of the Australian therapeutic goods industry is provided in box 4.1.

The TGA carries out a range of assessment and monitoring activities to ensure therapeutic goods available in Australia are of an acceptable standard. TGA is concerned with ensuring the quality, safety and efficacy of therapeutic goods (but not cost effectiveness). It charges, on a full cost recovery basis, for services provided to industry, such as processing of applications for inclusion on the Australian Register of Therapeutic Goods (ARTG), good manufacturing practice audits and annual licensing.

Figure 4.1 Current Health Technology Assessment Processes in Australia, Simplified



Adapted from Productivity Commission *Research Report 2005, Impacts of Advances in Medical Technology in Australia*, Overview, page XLVII.

Note: for clarity, the HTA conducted by private hospitals, private health insurers, and for special access schemes have been excluded from this figure. Also excluded are the interactions between public and private hospitals. Note that the Departments of Veterans Affairs and Health & Ageing administer services specifically for veterans which also may involve HTA.

Source: Department of Innovation, Industry, Science and Research.

Box 4.1 Australian therapeutic goods industry

Medicines

The Australian medicines industry spans a range of activity from human-use prescription medicines through to the production of generic over the counter medicines and complementary medicines — which includes herbal medicines; vitamin, mineral and other nutritional supplements; traditional and homoeopathic medicines. It includes Australian-owned companies and international companies with headquarters overseas.

The Australian pharmaceutical medicines industry:

- comprises approximately 1 per cent of the world market, with turnover of \$18 billion
- employs 40 000 people across at least 300 firms and institutions, including manufacturing, research and wholesaling — approximately 14 000 employed directly in the pharmaceutical manufacturing industry
- supplies 80-90 per cent of its output via the Pharmaceutical Benefits Scheme (PBS) to individuals, but there is also a large supply via hospitals
- is concentrated, with the top 20 companies (primarily large multinational corporations) accounting for more than 85 per cent of PBS sales
- exports were approximately \$3.9 billion in the 12 months to December 2007, making pharmaceuticals Australia's second largest manufactured export (DIISR 2008)
- spent around \$752 million on research and development in 2005-06 (DIISR 2008) — medicines typically have a long investment recovery period.

Reliable statistics on the complementary medicines industry are hard to find because of definitional difficulties and no comprehensive survey has been carried out. However, a handful of large companies dominate product manufacture and supply, with the remainder of the industry comprising a large number of very small companies. Total retail sales are in excess of \$1 billion.

Medical devices/technology

The medical technology industry in Australia has an annual turnover of \$4.75 billion and earns an export income of \$1.75 billion (in 2006-07). The industry comprises a small number of global multinational companies (approximately 20 per cent of the industry) and a large number of small and medium sized enterprises (80 per cent of the industry). The Australian market is small — less than two per cent of the global market for medical technologies (MTAA, sub. 23, p. 2). The industry has at least 10 000 employees in about 1100 companies. Australia exports most of the medical devices produced, yet imports most of the medical devices consumed. Medical devices typically have a short investment recovery period.

Sources Medicines Australia, sub. 35, pers. comm., 5 February 2008 and (<http://www.medicinesaustralia.com.au/pages/page4.asp>, accessed 5/2/08); Medical Technology Association of Australia, sub. 23, DIISR 2006, DIISR 2008, DIISR, pers. comm., 8 August 2008, DITR 2006.

The TGA also aims to ensure that the Australian community has access, within a reasonable time, to therapeutic advances and that unnecessary business compliance costs are avoided.

The regulatory framework is based on a risk management approach designed to ensure public health and safety, while at the same time freeing industry from any unnecessary regulatory burden. (DOHA 2008a)

It is evident from submissions that industry participants clearly recognise that any initiatives aimed at reducing regulatory burden must not compromise the need to maintain appropriately high standards of public health and safety.

Therapeutic goods are broadly divided into medicines and devices. In 2002, new regulatory arrangements for devices were introduced which differed in significant ways from the arrangements that continued to operate for medicines. The rest of this section outlines regulatory arrangements for medicines. Devices regulation is covered in section 4.3.

Medicines regulation

Australian manufacturers of medicines must hold a licence that is issued by the TGA. To obtain a licence the manufacturer must demonstrate adherence with internationally recognised manufacturing principles in the Australian Code of Good Manufacturing Practice (GMP).¹ The principles cover how medicines should be made, the standards that should be adhered to and the processes in place to provide assurance that each batch of a therapeutic good is safe and reliable and of consistent high quality. Before a licence is granted, Australian manufacturers are subjected to an audit by the TGA and, once licensed, are regularly audited to ensure that necessary standards are maintained. Overseas manufacturers of medicines imported into Australia are required to operate to standards equivalent to those expected of Australian manufacturers. They are either subject to similar licensing requirements in their own country (and the TGA makes an assessment of specific documentation) or they are audited by TGA inspectors where necessary.

Under the approval process, all medicines are required to be included in the ARTG before they can be supplied in Australia.²

¹The Australian Code is based entirely on the international standard published by the Pharmaceutical Inspection Co-operation Scheme (PIC/S) which is harmonised with the EU Guide to Good Manufacturing Practice for Medicinal Products and its Annexes.

² The ARTG is a computer database of information about therapeutic goods for human use approved for supply in, or exported from, Australia. Some goods captured by the Act are classified as 'exempt goods' and are not entered on the ARTG.

The Register has two parts: one for ‘registered goods’ and the other for ‘listed goods’. In general, medicines are:

- ‘registered’ if assessed as having a higher level of risk (prescription medicines and some non-prescription medicines), requiring rigorous and detailed examination of quality, safety and efficacy by the TGA before market entry³ or
- ‘listed’ if they are lower risk medicines (consumer medicines purchased over the counter such as complementary medicines, including herbal, vitamin and mineral products) requiring an assessment of quality and safety by TGA.⁴

The Act, regulations and orders set out the requirements for inclusion of medicines in the ARTG, including advertising, labelling, product appearance and appeal guidelines. Products are issued with a certification of registration or listing prior to supply.

An independent statutory body – the Australian Drug Evaluation Committee provides advice to the Minister and the Secretary of DOHA, through the TGA, on the suitability for marketing of prescription medicines in Australia, including:

- the quality, risk-benefit, effectiveness and access within a reasonable time of any medicine referred to it for evaluation
- medical and scientific evaluations of applications for registration of prescription medicines (for example, new chemical entities, new forms of previously registered medicines and therapeutic variations to registered medicines).

Post marketing monitoring and surveillance by TGA concentrates on checking safety and efficacy of products already on the Australian market through systems of adverse drug reactions and problem reporting, laboratory testing, and surveillance of product advertising. There are a variety of mechanisms for this task including the Adverse Drug Reaction Committee.

Some regulatory provisions, such as the scheduling of substances and the safe storage of therapeutic goods, are covered by the relevant state or territory legislation.

³ This requires manufacturers or importers to provide comprehensive scientific data to the TGA, which carries out independent assessments of the data. The main considerations are pharmaceutical chemistry and toxicological studies undertaken prior to the conduct of clinical trials and assessment of data from clinical trials.

⁴ In assessing the level of risk, factors such as the strength of a product, side effects, potential harm through prolonged use, toxicity and the seriousness of the medical condition for which the product is intended to be used, are all taken into account.

Pharmaceutical Benefits Scheme

Most prescription medicines in Australia are supplied through the Pharmaceutical Benefits Scheme (PBS). The Government subsidises PBS medicines so as to allow Australian patients access for a low standardised patient co-payment. Medicines have to be registered before they can be considered for inclusion on the PBS.

The Pharmaceutical Benefits Advisory Committee (PBAC) makes recommendations to the Minister about which medicines, medicinal preparations and vaccines should be listed on the PBS. The PBAC is an independent expert body established under the *National Health Act 1953* and its membership includes medical practitioners, pharmacists, consumers and health economists. It is supported by two sub-committees:

- the Drug Utilisation Sub-Committee, which primarily advises the PBAC on use and financial forecasts for major medicine submissions
- the Economics Sub-Committee, which primarily advises the PBAC on cost effectiveness aspects of major medicine submissions.

In submissions to the PBAC companies are required to do a full evaluation, providing evidence of the efficacy and safety of a new patented medicine as well as a cost-effectiveness analysis demonstrating that having the medicine on the PBS represents value for money for the taxpayer.⁵ The PBAC's assessment is based on the submission of the company and an evaluation by an external academic group.

If the PBAC recommends the product for listing on the PBS, then the information is sent to the Pharmaceutical Benefits Pricing Authority (PBPA) which makes recommendations to the Minister on the price and conditions of supply under the PBS. Companies have to make submissions to the PBPA and engage in pricing negotiations.

Within the PBS there are specifically defined therapeutic groups of medicines which have similar safety and health outcomes. Within these groups, the medicines can be interchanged at the patient level. If the PBAC's analysis merely establishes equal effectiveness, then consistent with the objective of minimising costs, a newly listed medicine's initial reimbursement price is linked to the lowest in the relevant price reference group. The difference in price between the lowest priced medicine and higher priced medicines within the group is called a therapeutic group premium, this is paid by the patient. There is always at least one drug within each group of

⁵ Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.2, December 2007) (DOHA 2007a).

medicines available without a premium. The PBPA reviews the PBS price of every listed medicine at least once a year based on their therapeutic group.

Marketing of medicines is heavily regulated, including how medicines can or cannot be marketed to the community and health professionals. There is a ban on the advertising of prescription medicines direct to consumers.

4.2 Concerns about regulation of medicines

Numerous specific concerns were raised about the regulation of medicines by a small number of participants. Taken as a whole, the issues suggest the need for significant reforms to improve the timeliness, transparency and consistency of assessment and approval processes, in particular the time taken from registration of medicines to eventual PBS listing. More efficient and timely processes have the potential to:

- reduce compliance burdens and lost marketing opportunities for business
- reduce administration costs for regulatory agencies, resulting from current overlap and other inefficiencies
- provide quicker public access to innovative medicines with potentially significant health benefits and savings in public health costs.

Many of the concerns have been recognised by previous reviews and in some cases the Government had agreed to the need for changes. However, progress in implementing reforms to address these unnecessary burdens has been slow.

In addition to the specific concerns raised, Pfizer (sub. 31) Australia emphasised the need for better compliance by the various regulators that govern its activities with regulatory best practice principles more generally, including:

- fairness
- transparency
- consistency in decision making and advice
- accountability
- a focus on outcomes
- creating certainty for all stakeholders
- decisions about the quality, safety, efficacy and cost-effectiveness of medicines should be based on objective scientific evidence and on rigorous statistical methods

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- duplication should be minimised and, where possible, eliminated.

Requirement for multiple ethics approvals

Pharmaceutical companies that undertake clinical trials in multiple states/territories in Australia need to obtain ethics clearance from the respective human research ethics committees in each jurisdiction.

Medicines Australia claimed that this ‘adds unnecessary burden on the industry in having to navigate its way through the different regulatory and approval processes as the applications for clinical trials need to be tailored for each jurisdiction’ (sub. 35, p. 5).

Assessment

Scientific and ethical reviews of research proposals are important steps in the approval of research involving humans in Australia.

Research on humans is approved by human research ethics committees before being allowed to commence. Where approvals from multiple ethics committees are required the process can impose significant unnecessary compliance costs for companies. It can also cause delays that slow access to new treatments and, in extreme cases, can lead to the abandonment of research.

The National Health and Medical Research Council (NHMRC) – an independent statutory agency, which provides advice on ethical behaviour in health care and in the conduct of health and medical research, including research involving humans (clinical trials) – has been working on a number of initiatives to make the research approvals process more efficient and effective.⁶ In particular, the Australian Health Ministers Advisory Council agreed in October 2006 that the NHMRC should establish a process for the harmonisation of multi-centre ethical review.

The NHMRC is not involved in the operational aspects of conducting reviews, but has been charged with developing a framework for the harmonisation of reviews involving multiple research centres. NHMRC’s work is informed by a reference group which includes Medicines Australia. The 2007 Federal Budget made \$5.6 million available to the NHMRC to establish a coordinated *national* system to

⁶ The NHMRC Australian Health Ethics Committee advises the NHMRC on ethical issues relating to health and develops guidelines to ensure that research is conducted in a professional and ethical manner. More broadly, the NHMRC is Australia’s principal agency for funding health and medical research and for developing health advice for the Australian community, health professionals and governments.

streamline ethics reviews of cross-jurisdictional and multi-centre human research (NHMRC 2007).

A number of jurisdictions already have or are moving to establish human research ethics committees that are able to provide appropriate ethical and scientific review on behalf of all participating institutions *within* their jurisdictions. NSW was the first State to introduce a streamlined, multi-centre ethical approval process and there has been some evidence that ethical approval times have improved. Whilst such state initiatives are welcome, a coordinated nationally harmonised system is likely to maximise efficiency gains.

A consultant was commissioned by NHMRC to help develop an implementation plan and a report was presented to NHMRC in July 2007. The Pittman Report confirmed the importance of reform in this area:

A change to improve the process of approval for multi-centre research is critical, with Australia lagging behind other developed economies. In the UK, for example, multi-centre research ethics committees were formally established in 1997. (Pittman 2007, p. 4)

In its submission in response to the Commission's draft report, Medicines Australia acknowledged the work of the NHMRC and offered its ongoing support, but expressed concern about the lack of tangible progress since the release of the Pittman Report.

... there is a real need to urgently push forward with a national streamlined approach to multi-centre clinical trial approval as soon as possible. Medicines Australia calls for a clear work-plan and timeline for implementation to be set so that the new system should be ready to commence early in 2009. It is disappointing that the harmonisation work has not been completed, particularly given that NHRMC was explicitly given funding by the Federal Government in 2007 to complete this work. (Medicines Australia, sub. DR64, p. 6)

The NHMRC (sub. DR 63) provided an update on the status of the harmonisation project, including information on timelines and key commitments, including a commitment to full implementation by 2009-10. Currently NHMRC is conducting focus groups in all states and territories to determine stakeholder views on the critical elements of a harmonised system. Some of the issues being considered, include:

- recognition/accreditation of ethics committees
- insurance and indemnity
- costs and fees.

NHMRC has also committed to providing updates on the project on its website.

A more centralised ethics approval process will reduce red tape and other compliance costs and facilitate faster access to new medicines. The Commission notes the current work of the NHMRC and encourages all governments to achieve full implementation of a national system by no later than the 2009-10 timeframe commitments set out by the NHMRC.

Timeliness and cost of manufacturing audits/GMP assessments

Various concerns were raised relating to TGA processes for assessing manufacturers' compliance with Good Manufacturing Practice (GMP), including:

- the cost and time taken to conduct audits or desktop assessments can be excessive and uncertain:

Companies are frequently left waiting for months for such assessments ... Often the current GMP clearance has expired. Finally when clearances are received, they have short expiry times requiring companies to make new applications within a short time-frame. This is time and labour intensive as well as a costly regulatory burden. (Medicines Australia, sub. 35, p. 4)

The ability to recoup the application fee (many thousands of dollars including additional resources to prepare an application) as well as overall uncertainty of approval timeframes discourages new ingredient applications ... Although an extraordinary example ..., CHC submitted, on behalf of a number of members ... an application for a new ingredient (widely used as a traditional medicine overseas) for use in listed medicines in June 2003. The ingredient was gazetted for use on 31 July 2008; i.e. 5 years later. (Complementary Healthcare Council of Australia, sub. DR68, p. 3)

- insufficient recognition of overseas GMP audits/assessments audits are repeated throughout many global regulatory authorities, but information is rarely shared and TGA is duplicating inspections conducted by overseas authorities (Medicines Australia, sub. 35).

For Pfizer, as a major international manufacturer, all of these additional requirements create significant duplication of effort. Plants now spend a great deal of time preparing for and participating in GMP audits. Currently, plants may be inspected by a European Union authority and a USA authority and now the TGA can insist on inspecting the same site for exactly the same processes.

Our core concern beyond the cost and inconvenience and uncertainty of multiple inspections is that the principle of inspection has been lost. We have a duplication of effort and an increase in uncertainty for no increase in outcome (that is, safety and quality). (Pfizer, sub. 31, pp. 7-8)

There is concern that the recently revised ... Guidelines ... will lead to a significant increase in the number of actual overseas audit visits by MAB [Manufacturing Assessment Branch, now known as the Office of Manufacturing Quality]. This will add

a considerable cost, time and regulatory burden to industry. (Medicines Australia, sub. 35, p. 4)

- uncertainty around expiry date for GMP clearances there has been a recent change by TGA from expiry 3 years from last inspection to expiry based on a risk matrix which they do not make available to industry (Pfizer, sub. 31).
- difficulties obtaining documentary evidence of a standard acceptable to the TGA for desk-top audits of overseas manufacturing plants including problems obtaining Establishment Inspection Reports (EIR), scope and confidentiality issues (reports are often edited and the TGA will not accept an edited EIR) (Pfizer, sub. 31, pp. 6 7).

In comments on the draft report, Johnson and Johnson Family of Companies (sub. DR70) stated that it generally shared the above concerns and also raised the following additional concerns:

- inconsistencies in the risk minimisation approach adopted by the Office of Manufacturing Quality:

... due to the TGA's inability to efficiently process large volumes of desktop audits applications, they have been granting, on a case-by-case basis, extensions of expired Clearances. Similarly, due to the shortage of auditors available to perform overseas manufacturer inspections, the TGA have been issuing GMP Pre-Clearances without prior inspection. Such practices, are inconsistent with the risk minimisation approach that the TGA is striving to adopt. Additionally, we feel that the TGA should not be implementing requirements that they do not have the adequate resources to cope with. (sub. DR70, p. 10)

- short response timeframes when random TGA inspections are announced (a similar concern was also raised by Pfizer in its comments on the Draft Report (sub. DR53)):

... when Janssen-Cilag [part of the Johnson & Johnson Group] was informed of a random inspection initiated by the TGA, we were given a very short timeframe (5 working days) in which to respond. This is of concern given that the typical cost of audits may range in the tens of thousands of dollars and sometimes into the hundreds of thousands, depending on the duration of the inspection as well as the number of TGA representatives performing the inspection. Decisions involving such large sums cannot easily be made, particularly in the case of multinational companies where input may be required from Head Office. (sub. DR70, p. 10)

Assessment

The TGA audits Australian manufacturers before a licence is granted, to ensure their production procedures comply with internationally recognised GMP principles

and then regularly inspects licensed manufacturers to ensure that necessary standards are maintained.

Overseas manufacturers of medicines imported into Australia are required to operate to standards equivalent to those expected of a licensed Australian manufacturer. A Sponsor⁷ applying to the TGA for registration or listing of therapeutic goods manufactured outside Australia, in the absence of a TGA audit, must provide documentary evidence to show that the manufacture of the goods is of an acceptable standard. Sponsors of therapeutic goods manufactured outside Australia must obtain GMP Clearance for the overseas manufacturer(s) before the goods are entered on the ARTG.

Documentary evidence is assessed by the TGA through a 'desktop audit' process. If acceptable documentary GMP evidence cannot be provided, the TGA will undertake on-site audits in the same manner as that conducted for the Australian manufacturers.⁸

Australia participates in several international arrangements including Mutual Recognition Agreements (MRAs), the Pharmaceutical Inspection Cooperation Scheme (PIC/S) and other arrangements that provide for the exchange of regulatory information. The countries of the regulators who are recognised participants in an MRA (or equivalent) with Australia include the EC and EFTA Countries,⁹ Canada, Singapore, and Switzerland (arrangements generally equivalent to an MRA).

The TGA has an agreement with the US Food and Drug Administration (US FDA) that provides for the exchange of information in relation to manufacturers for regulatory purposes.

The TGA recently revised its Guidance for Sponsors and manufacturers on the GMP clearance of overseas medicine manufacturers.¹⁰ Medicines Australia and Pfizer both expressed concern that changes in the latest edition of the Guidance document will significantly increase the number of duplicative inspections and consequent unnecessary compliance costs for business and administration costs for the TGA.

⁷ 'Sponsor' is the person, business or company that has the prime responsibility for the supply of the product in Australia. The Sponsor may also be the manufacturer of the good.

⁸ The term 'audit' is generally used in Australia, whereas overseas regulatory agencies may use the term 'inspection'.

⁹ Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Liechtenstein, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden.

¹⁰ Guidance on the GMP clearance of overseas medicine manufacturers, 16th edition, March 2008, (DOHA 2008b, available at <http://www.tga.gov.au/manuf/gmpsom.htm>).

A number of the changes to GMP clearance of overseas medicine manufacturers initiated in recent years by the TGA have been in part a response to the Performance Audit Report of the Australian National Audit Office into *Regulation of Non-prescription Medicinal Products* (ANAO 2004). The Audit raised significant concerns about the standard and timeliness of assessments of overseas manufacturers. Notwithstanding that the report did not deal directly with regulation of prescription medicines, many of the findings and recommendations of the Review were equally of relevance to these medicines. The Audit found:

The TGA has a structured framework for the regulation of risk ... However, more rigour around systems, procedures and resource management within the framework is required to provide assurance that non-prescription medicines are appropriately and cost-effectively regulated. (ANAO 2004, p. 19)

And recommended:

... that the Department of Health and Ageing review and improve the TGA's quality assurance program to improve the quality, consistency and reliability of its GMP audits. (Recommendation No. 25) (ANAO 2004, p. 28)

The recently revised GMP clearance guidance document provides the following information in relation to acceptable documentary evidence:

- the TGA will accept Certificates of GMP Compliance, issued under the provisions of an MRA (for types of products covered by the MRA), where the manufacturer is located in the same country as a Regulator that is a recognised participant in the MRA
- the scope of an MRA does not include audits conducted in countries outside the country of an MRA Regulator

Audits and GMP Certification, from MRA Regulators, for manufacturers in third countries will no longer be automatically accepted. This is because audits in these countries may not include all aspects of the manufacture of medicines for supply to Australia (DOHA 2008b)

- GMP Certification from PIC/S member countries are not automatically accepted; the only exceptions to this is where the Regulator in the PIC/S member country is also a Regulator who participates in an MRA with Australia, and the certificate is issued under the provisions of the MRA
- GMP Clearance is not automatically granted to Sponsors of US manufacturers inspected by the US FDA or New Zealand Medsafe.¹¹

¹¹ Under the Trans Tasman Mutual Recognition Arrangement, generally goods that can lawfully be sold in New Zealand can also be sold in Australia. However, therapeutic goods are one of six sectors covered by a special exemptions. The Commission is currently undertaking a review of the mutual recognition schemes.

Where documentary evidence is submitted under the provisions of an MRA, a brief assessment is typically undertaken. In all other cases a desktop audit of the documentary evidence is conducted.

Whereas some overseas regulatory authorities (for example the US FDA) are required to conduct their own inspections for all overseas plants supplying to their domestic market, the TGA endeavours to minimise the number of overseas inspections and will not conduct its own inspection where suitable evidence to demonstrate acceptable GMP compliance is received. Given the TGA's full cost recovery arrangements, this policy substantially reduces regulatory compliance costs for sponsors in Australia, since the direct cost of desk-top audits are generally only a small fraction (less than one tenth) of the cost of a full on-site GMP inspection. Further, indirect costs to businesses of preparing and participating in an audit inspection (including staff time costs) are substantial.

The TGA has an obligation to ensure that documentary evidence provided by sponsors is of sufficient quality to provide the necessary assurance of an overseas manufacturer's compliance with GMP. One aspect of assessing the quality of the evidence is ensuring that it is relevant in its scope. One reason that the TGA will not automatically issue GMP clearances for sites inspected by the US FDA is that the FDA generally limits the scope of its inspections to products and processes which impact on medicines approved and marketed in the US. The TGA has a statutory obligation to ensure there is evidence that the relevant factories (buildings) on the site that are manufacturing products for Australia were inspected and cleared by FDA inspectors.

The medicines industry did not argue that the TGA's evidentiary requirements are unreasonable and in roundtable discussions acknowledged that evidence submitted by industry to the TGA was on occasions of a poor standard. Many of the concerns raised by industry about problems obtaining the required evidence are generally beyond the control of the TGA. The TGA should continue to work with companies to try to improve the quality of reports from overseas subcontracting plants and facilitate access to inspection reports. As a further initiative, the Commission sees merit in the TGA preparing an advisory document listing common deficiencies in applications for desk top audits, as suggested by Medicines Australia (sub. DR64) so as to reduce the incidence of delays or rejections, due to unacceptable evidence, that could have been anticipated by the sponsor.

While the Commission acknowledges that outside the MRA countries, a case by case assessment may generally be appropriate when assessing the evidentiary or audit requirements for GMP Clearance, there would be significant cost savings for many pharmaceutical companies if the TGA were to more widely recognise prior certification processes conducted overseas by bodies assessed as suitably

competent. The TGA Office of Manufacturing Quality (formerly the Manufacturing Assessment Branch) has a current initiative to identify where manufacturing audit results may be shared between global regulatory authorities and to improve communication of audits and this may lead to some greater recognition and acceptance of overseas GMP assessments. DOHA has advised:

The TGA is initiating improvements in international regulation of GMP. The TGA's 'Smart GMP Regulation' initiative is in the vanguard of international work to enhance inter-regulator communication and information exchange, actively addressing unnecessary duplication of inspections of medicine manufacturers. Other international regulators are working with the TGA to adopt our GMP regulatory approaches to collectively ensure that regulators do not unnecessarily duplicate inspections of medicine manufacturers in any specific part of the world. (pers. comm., 5 June 2008)

The TGA has also recently joined with the US FDA and the European Medicines Agency (EMA) in a pilot project designed to facilitate collaboration on inspections of active pharmaceutical ingredients manufacturers in third countries. The pilot project provides for sharing of information on inspections between the TGA, US FDA and the EMA and rationalisation of international GMP inspection activities. DOHA stated that 'should the pilot project demonstrate that it is an effective mechanism for improving the efficiency of GMP inspections, further international collaborative inspection programs are likely to be developed' (DOHA, sub. DR71, p. 4).

In relation to complementary medicines, the Commission notes that any move to recognise more widely prior overseas inspections/assessments may not significantly reduce compliance costs for manufacturers in Australia. This is because many overseas regulatory agencies (including the US FDA) do not audit complementary medicine manufacturers supplying their market, since these products are not regulated as 'medicines'. As one option for reducing costs and improving timeliness of access to complementary medicines, the TGA should examine the feasibility of using competent overseas-based third party accredited auditors as an alternative to sending TGA auditors. Any examination would need to establish the scope for such a change to result in significant cost savings that could be passed on to businesses. This was suggested by the Complementary Healthcare Council of Australia (sub. DR68), but might have wider application to prescription medicines, possibly after a trial implementation period for complementary medicines.

Timeliness

In relation to concerns about the time taken to conduct audits, the Commission understands that Australian inspections are given the highest priority and according to the TGA are 'always conducted on time' (TGA, pers. comm., 1 August 2008).

Overseas inspections of manufacturers of medicines are prioritised taking into account available resources. The TGA acknowledges that ‘from time to time inspections ... that have no impact on national supply can be delayed’ (TGA, pers. comm., 1 August 2008).

The Commission accepts that there may be times when it is appropriate for the regulator to insist on an inspection on short notice. But where the regulator is open to the alternative of a desk-top assessment based on suitable documentary evidence, companies should be allowed sufficient advance notice in order to investigate the feasibility of opting for that less costly alternative.

The Office of Manufacturing Quality within the TGA is working to reduce waiting periods for processing of desktop audits. It is currently conducting an internal review of processes and recruiting additional staff, including GMP inspectors. While this should go some way to addressing delays, the Commission is concerned that the TGA has not committed to specific GMP Clearance timeframes – with the exception of MRA certification where the Guidance document gives a rather loose commitment that ‘the processing of the application will generally be completed within fifteen (15) working days’ (DOHA 2008b, p. 16). Where non-MRA certification and supporting documentation is submitted as evidence the assessment (desktop audit) and decision process ‘will be completed as soon as possible’ (DOHA 2008b, p. 16). In advice to the Commission, DOHA stated:

‘Desktop audits’ are not constrained by legislated timeframes as significant additional costs would be borne by industry for additional resources (GMP inspectors) to meet these timeframes. (pers. comm., 5 June 2008)

While acknowledging that faster processing may imply some additional charges for industry, these must be balanced against the substantial benefits associated with being able to get products into the marketplace quicker.

The time taken to conduct assessments should, at a minimum, be constrained by a strong written commitment by TGA to specific timeframes, negotiated with industry and with any cost trade-offs made transparent. There would need to be some flexibility to deal with special circumstances and ‘stop the clock’ provisions to make allowance for delays in the provision of evidence that are beyond the control of the TGA.

Uncertainty of expiry dates

In relation to specific concerns about *uncertainty* of expiry dates for GMP clearances, the Commission notes that the TGA’s policy is as follows:

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- for GMP clearances issued on the basis of an MRA Certificate of GMP Compliance, the GMP Clearance remains current until the date of expiry on the MRA Certificate, unless the TGA has documentary evidence to vary the expiry date
 - for other GMP Clearances, the expiry depends on the type of product manufactured and the outcome of the desktop assessment process. The period of GMP Clearance is determined using a risk-based criteria similar to that used by the TGA to determine the re-audit period for any manufacturer (domestic or overseas) audited by the TGA, so as to be ‘consistent with the TGA’s “level playing field” approach to GMP regulation’ (DOHA 2008b, p. 10).

Previously, a GMP Clearance for an active pharmaceutical ingredient or finished product would expire three years from the date of the last audit. Pfizer’s concern is that under the new risk-based approach, expiry dates will be reduced. This would generate additional compliance costs associated with more frequent applications, and the number of TGA audits will increase. More fundamentally, Pfizer has concerns about the uncertainty created by the new approach:

Now the TGA has indicated that it will calculate expiry dates using a risk matrix. However, the TGA will not make this risk matrix available to industry, and manufacturers like Pfizer Australia have no way of determining what length of clearance they will receive for subcontracted plants overseas. (sub. 31, p. 7)

Once the re-inspection period is determined using the risk matrix, GMP clearance is issued for that period of time, plus six months, to allow for the TGA inspection to be scheduled and conducted.

Consistent application of risk criteria to Australian and overseas manufacturers supplying the Australian market does establish a ‘level playing field’, in one sense. But greater consideration also needs to be given to the requirements Australia is placing on its domestic manufacturers and overseas plants supplying the Australian market relative to requirements imposed by other developed countries that seek to maintain similarly high standards of safety for medicines supplied to their domestic market, for example the US and EC countries. According to Pfizer (sub. 31, p. 8) and Johnson and Johnson Family of Companies (sub. DR70, p. 10) Australian sponsors have a harder time registering overseas plants than pharmaceutical manufacturers anywhere else in the world. In a similar vein, the Complementary Healthcare Council of Australia noted that complementary medicines are typically not regulated as ‘medicines’ internationally (and current MRA’s do not apply to complementary medicines), but the Commission notes that this reflects a difference in policy and so is outside the scope of this study.

Further, the risk-based criteria used to determine expiry dates should be more transparent, ideally via publication on the TGA's website, such that Sponsors are able to reasonably anticipate the expiry dates that are likely to be determined for their GMP Certificates and plan accordingly. In comments submitted on the Commission's draft report, DOHA agreed:

... increased transparency could be achieved through publishing some details of the risk-based approach used by the TGA in its GMP processes, on the TGA website. The TGA will undertake to publish such information. (sub. DR71, p. 3)

In principle, the design of TGA's processes for assessing manufacturers' compliance with GMP have a high degree of consistency with best practice principles. They are based on a risk-management approach and a desire to minimise unnecessary business compliance costs and administration costs. Nevertheless, in practice, there is scope to improve the transparency, timeliness and consistency of application of audit processes, particularly the times and costs associated with overseas audits or desk-top assessments.

RESPONSE 4.1

The current reviews by the Therapeutic Goods Administration (TGA) need to achieve the following outcomes:

- ***a stronger commitment by TGA to timely audits/clearance processes, including by incorporating explicit timeframes into publicly available guidelines***
- ***improved transparency and consistent application of the risk-based criteria used to determine expiry dates for Good Manufacturing Practice (GMP) certificates***
- ***wider recognition of international processes and acceptance of GMP certificates where conducted by bodies assessed as suitably competent.***

TGA transparency and communication

Various concerns were raised regarding TGA's transparency and communication with stakeholders, including:

- a general lack of transparency (and certainty) in TGA processes '...we are not certain how or why the TGA makes decisions.' (Pfizer, sub. 31, p. 8)
- frequent changes to Guidance, and the imposition of new requirements without sufficient consultation with industry

This document [Guidance on the GMP Clearance of Overseas Medicine Manufacturers] has been updated 4 times in the last 2 years and only with the latest edition, i.e. the 16th edition, was industry given a small window of opportunity to comment. We believe that the TGA needs to take a true consultative approach in

adopting new/revised Guidelines by giving companies the opportunity and sufficient time to comment on changes and new requirements. In addition the TGA should allow for a transition period for new requirements to be operational. This would provide multinational pharmaceutical companies with sufficient time to familiarise their Head Office functions with the new requirements and to allow generation of new information to meet these additional requirements. (Johnson & Johnson Family of Companies, sub. DR70, p. 11)

- the system for registration requires hard copy submissions to the TGA.

The preparation of these hard copy submissions causes a burden on industry in the time taken to print, the cost of materials, the work in collating volumes of paperwork, as well as the transport and printing costs in providing this material to TGA. Having to review paper copies also increases the time taken for TGA to review submissions. Complex submissions to TGA often run to many volumes of paperwork. (Medicines Australia, sub. 35, p. 5)

Assessment

Although highlighting specific aspects of TGA's performance that need to improve, participants were keen to acknowledge the high standard of the TGA's work:

... the TGA's assessment of the medicines' quality, safety and efficacy is of the highest standard. The advice that our Australian manufacturing staff receive from the TGA following audits is also excellent. The TGA's policy work has been very good. (Pfizer, sub. DR53, p. 1)

And Medicines Australia noted that 'TGA has a very good international reputation' (Medicines Australia, sub. 35, p. 2).

Transparency of processes for making, changing, reviewing, communicating and then administering regulations is vital for ensuring regulatory efficiency and the control of business compliance costs. Affected businesses should be consulted and have adequate opportunity to contribute to the development and design of the regulation and associated administrative processes. Regulations and administrative decision making by the TGA must be clear, consistent and accessible.

The TGA publishes all requirements and guidelines and is required by legislation to meet prescribed timelines and provide reasons to applicants for decisions. The TGA's website has substantial, readily accessible information about regulatory requirements and administrative processes. As well as providing links to relevant legislation and regulation, Guidance documents are available covering various aspects of the Regulatory Framework that provide more detail on process and information requirements.

The TGA consults with industry on individual proposals and through standing arrangements, especially the Industry Consultative Committee. Consultative processes were improved following a review in 2003-04 (Evans, A. 2004). The Industry Consultative Committee provides a forum to exchange information on industry trends and regulatory expectations, to discuss the development of the TGA's corporate plan, annual business plans and budget. The TGA reviews its fees and charges each year and consults with stakeholders on proposed changes through the Industry Consultative Committee. Bilateral discussions are also conducted with industry associations on sector specific changes to fees and charges (pers. comm., 5 June 2008).

The TGA also conducts seminars and workshops for industry to facilitate better understanding of current regulatory requirements and proposed reforms. For example, in late July and early August 2008, the TGA held workshops for each of the four major therapeutic goods sectors on proposed regulatory reforms. These workshops have been welcomed by Medicines Australia, which stated that the consultations 'point to a renewed commitment on the part of the TGA to implement the workflow practices reforms' (sub. DR64, p. 2), but it also emphasised that the 'priority is now to ensure that the reforms are finalised and implemented in a timely manner and in partnership with the industry' (ibid).

For prescription medicines the TGA has a process for establishing or amending guidelines, which was negotiated with industry associations. Copies of the proposed guidelines are sent to the three key industry associations in the prescription medicines sector, who are asked to respond in a one to two month period. The associations then collate comments from their members and forward these to the TGA (pers. comm., 5 June 2008).

The TGA has recognised that there is the potential for efficiency gains through improved information technology capability and has initiated a project to enhance its IT capability. This includes facilitating electronic lodgement of submissions. The TGA informed the Commission that it expects to issue a tender for the IT support for the review of electronic submissions for prescription medicines before the end of this calendar year.

Overall, with respect to the transparency of TGA's regulation of *medicines*, the Commission did not receive conclusive evidence to confirm that there are widespread or systemic problems. Moreover, the Commission has identified a number of positive aspects of the TGA's communication and consultative processes. Nevertheless, the concerns that have been raised suggest there is scope to do better and this has been acknowledged by the TGA. The TGA should use the current internal process review being conducted by the Office of Manufacturing Quality to identify, in consultation with industry, further measures to improve the

regulator's transparency and communication with stakeholders. Outcomes should include ensuring that the reasons for decisions are always clearly communicated and that there are adequate opportunities for affected businesses to provide feedback on proposed reforms to regulation and associated administrative processes.

Concerns about PBS listing and pricing processes

The following specific concerns were raised in relation to PBS listing and pricing processes:

- lack of fairness and transparency in PBAC processes

‘mismatch of early advice on our PBAC submissions and the PBAC’s final recommendations’ advice given by the PBAC secretariat within DOHA is often not adequately reflected in the independent evaluation on which the listing decision is based or in the PBAC’s final recommendations to the Minister. (Pfizer, sub. 31, p. 8)

companies are allowed only ten minutes to address PBAC in relation to their submissions and following receipt of commentary from external academic groups, which is not commensurate with the complexity of submissions and the time involved in their preparation (Pfizer, sub. 31, p. 10)

under PBAC Guidelines manufacturers are allowed only five days to respond to evaluator’s comments (which are often more than 50 pages and highly technical), which ‘is quite disproportionate to the months that are spent preparing and evaluating submissions’ (Pfizer, sub. 31, p. 10) and currently PBAC posts commentaries by mail, reducing the already limited time to respond

- lack of accountability of PBAC evaluations manufacturers have limited opportunities to address errors of fact or major omissions

... an increasing number of elements in evaluations are simply wrong or contain major omissions, and consequently the PBAC is being given guidance that may lead to them incorrectly reject[ing] our medicines. Pharmaceutical manufacturers currently have only limited opportunities to address errors of fact or major omissions. While there is a review process, this can only assess the PBAC’s own processes, not the evaluation itself. (Pfizer, sub. 31, pp. 9 10)

- generally there is insufficient transparency around the PBAC evaluation process

... there are important parts of the evaluation system that are unclear to us: how many evaluators there are; what their workload is; how many submissions they typically evaluate for each sitting of the PBAC; how often they are replaced or rotated (if at all); what sort of feedback they receive from the PBAC and Pharmaceutical Benefits Branch; and how feedback is institutionalised amongst the body of evaluators. We also do not know how the responses we provide to the PBAC and its subcommittees are

actually handled by those groups and, most importantly, have no opportunity to interact with the evaluators during the evaluation process. It would certainly help us to know how the PBAC views those responses which point out errors in evaluations, and what formal processes it has for dealing with them. (Pfizer, sub. DR53, p. 3)

- PBAC is not allowing evaluators sufficient time to undertake complex evaluations (Pfizer, sub. 31, p. 10)
- the application of the Weighted Average Monthly Treatment Cost (WAMTC) method for reference pricing purposes generates substantial financial and administrative costs to both the Government and industry

A WAMTC review can take between 10 to 14 weeks. During this time, considerable resources are allocated by both Government and companies to collecting, collating and analysing data, followed by verification of the accuracy of the WAMTC calculation. The cost of purchasing data alone is prohibitive. For example, the costs of purchasing necessary data range from \$8000 and \$16000 for an ad-hoc WAMTC query. The total average cost thus amounts to between \$110 000-120 000 per annum for each company. Considering there are around seven WAMTC reviews each year, and any one review will have a number of companies involved each required to collect and submit their own data the compliance cost to the industry as a whole ... will be much higher. (Medicines Australia, sub. 35, p. 7)

In commenting on the Commission's draft report, Medicines Australia (sub. DR64), Pfizer (sub. DR53) and Johnson & Johnson (sub. DR70) also questioned the continuing need for the WAMTC policy in light of recent PBS reforms. Medicines Australia, for example stated:

The rationale of the PBS reforms is to encourage savings to the taxpayer by facilitating differential pricing for medicines with multiple brands where there is competition. WAMTC, by definition, is designed to equalise the price of different medicines it is inconsistent with the policy direction of the PBS. It is likely to be increasingly untenable in a competitive pricing environment with different prices for multiple brand medicines driven by PBS reform. This inconsistency and increasing irrelevance, coupled with the regulatory cost of WAMTC on companies, suggests that WAMTC should be abandoned as a methodology altogether. (Medicines Australia, sub. DR64, p. 5)

Assessment

In applying to have a medicine listed on the PBS, a company must submit to PBAC detailed clinical evidence (including safety toxicity, adverse reactions, etc) as well as an analysis of the cost-effectiveness of the medicine relative to alternatives. The submissions are complex and becoming more complex over time. According to Pfizer (sub. 31), the main reasons for this are that medicines are becoming more specialised with smaller patient populations. This means the trial data are more complex to evaluate and more sophisticated analytical methods are required. The

complexity and detail makes submissions costly and time consuming for companies to develop (submissions can take many months to prepare) and they also impose significant resource and expertise demands on evaluators. Submissions to PBAC and PBPA:

... can impose a significant regulatory burden on ... companies ... particularly for complex submissions, such as where there is a request for further information or clarification is required, or where a medicine has been rejected previously and requires multiple resubmissions in order to achieve a positive recommendation from PBAC. ... [it] can be quite a resource intensive process. (Medicines Australia, sub. 35, p. 6)

PBAC and PBPA must have sufficient resources and time to evaluate submissions so as to avoid errors or omissions that can be very costly both to companies and potentially in terms of health outcomes for the community. The volume of submissions to PBAC has been growing in recent years and this together with the increasing complexity of submissions would have significantly increased the workload of PBAC.

In 2000, each PBAC meeting made around 15-25 recommendations to list medicines on the PBS; in November 2007, they recommended 53 medicines for listing. Despite this increase, the PBAC has not advertised any increase in the time devoted to evaluations, or in specialist subcommittees or in PBAC meetings. (Pfizer, sub. 31, p. 11)

To address this, provision has been made in the legislation to increase the membership of the PBAC from 12 to 18 members and the length of the scheduled PBAC meetings has recently been increased to three days (from one to three days previously). However, the number of meetings per year has been reduced from four to three. The PBAC also holds separate one-day extraordinary meetings to deal with other matters, but these meetings have typically dealt with a very small number of assessments.

Companies must also be given sufficient time to respond to feedback/commentaries on their submissions. In this regard, some aspects of PBAC procedures and processes do *prima facie* seem unnecessarily burdensome. This is particularly evident with respect to the extremely short time (five days) that companies are given to respond to evaluators' comments, especially in light of PBAC's insistence that the comments be sent to the company by post.

DOHA have informed the Commission that commentaries are sent in hard copy so that commercial-in-confidence material can be appropriately blacked out (pers. comm., 5 June 2008). The Commission considers that commentaries should be transmitted electronically consistent with the requirement imposed on manufacturers to make submissions in a useable electronic format. The PBAC Secretariat should explore technical options that would enable electronic transmission while ensuring confidential material cannot be accessed in electronic

files. At a minimum ‘portable document file’ (PDF) files (with blacking out) could be sent rather than hard copies in the mail.

Based on DOHA’s description of current processes it would appear that there are opportunities for sponsors to address errors of fact or omissions, including in the reports of the contracted evaluators:

If the sponsor has correctly identified in its pre-sub-committee response that errors of fact or omissions exist in the evaluation report, the errors are documented and tabled at the sub-committee meeting. The errors are then formally acknowledged and specifically brought to the attention of the PBAC, and the sponsor, as part of the minutes of the meetings. The evaluators receive the comments from the sponsors to the evaluation reports. The groups also receive general feedback on their performance as part of usual contract management between the Pharmaceutical Evaluation Branch and the academic evaluation groups.

The sponsor is provided with a copy of the [Economics Sub Committee] Advice to the PBAC and has a further opportunity to comment in a pre-PBAC response.

The sponsor of a major submission can also request a hearing at the PBAC meeting. The scope and duration of the hearing before the PBAC have been extensively discussed and jointly agreed upon by the Department of Health and Ageing and the pharmaceutical industry, represented by Medicines Australia, as part of the implementation of the Australia United States Free Trade Agreement. (DOHA, pers. comm., 5 June 2008)

However, the concerns raised by Pfizer (including further elaboration in a supplementary submission, DR53) suggest the need for a further examination of the adequacy of current review opportunities and the process of ensuring that any significant errors, including in evaluators reports, are corrected. There appears to be a case for allowing companies additional time to present at PBAC hearings. As a first step, however, there is a need for DOHA to more clearly communicate review opportunities that exist within current processes and, more generally, to enhance the transparency of the whole PBAC evaluation processes.

Typically, before a manufacturer lodges a major PBAC submission it holds preliminary discussions with officers from the Pharmaceutical Benefits Branch (PBB) of the DOHA, which provides secretariat and technical support to the PBAC. The initial meetings with the PBB can help to ensure that the time consuming process of preparing the submission is as focused and efficient for the company as possible. Pfizer stated in their submission that such meetings are an opportunity for both sides to ‘discuss issues with clinical evidence, determine the comparator, and discuss approaches to the PBAC if there is a rejection’ (Pfizer, sub. 31, p. 9). DOHA told the Commission that meetings are used to:

... discuss aspects of data collection, submission preparation, PBAC considerations and pricing matters, and other related issues. These meetings aim to assist in the listing

process, and encourage cooperative working arrangements with pharmaceutical companies. (pers. comm., 5 June 2008)

The advice of PBB is non-binding on evaluators and PBAC so it is possible for submissions to be rejected or deferred, notwithstanding that early advice provided by PBB has been followed.

Judgements must be made on the basis of the totality of available clinical and economic evidence, by PBAC after an independent assessment by evaluators and consideration by PBAC sub-committees. A system that sought to make preliminary advice of the Department binding would appear unworkable, in effect making the Department the decision maker, rather than PBAC. Even something less than binding is likely to make the Department reluctant to provide any early advice. This would overall be to the detriment of companies that benefit from early consultation and feedback on their proposed submissions. This position was accepted by Pfizer in its comments on the draft report (sub. DR53).

The Commission considers that the preliminary meetings with the PBB serve a useful function, particularly in relation to ensuring procedural and information requirements are clearly understood. The costs of avoidable re-lodgements can be very high for companies so there is an onus on DOHA to ensure that any preliminary advice given in relation to the evaluation method, data requirements or other process matters is well considered and as accurate as possible.

Pfizer suggested that an agreed record of the advice given by PBB with respect to the evaluation method the sponsor should use should be included with the submission so that the evaluator is aware of that advice. Therefore any decision by the evaluator to select a different evaluation method would not be one taken lightly. This suggestion has some merit and may serve to enhance transparency and accountability. However, any consideration of whether to make this a requirement would need to take into account additional administrative costs for PBB and the potential either to constrain their advice or to place pressure on the independent evaluators to select a method consistent with the PBB advice.

Several participants raised concerns about aspects of the Weighted Average Monthly Treatment Cost (WAMTC) methodology. For medicines that have been assessed as being of equivalent safety and efficacy for a common clinical indication, a 'Reference Pricing Policy' is adopted and the WAMTC is a method of calculating a benchmark or reference price for groups of related medicines, using clinician prescribing data. There are currently six WAMTC groups which are each composed of medicines that provide the same or similar health outcomes.

Regular reviews of the cost-effectiveness of medicines are necessary to ensure that the Government and taxpayers get the best value from the PBS. Medicine prices may need to be changed, for example, if actual patterns of use differ from that predicted or if post-marketing evidence shows that a medicine has worked better or worse than it had in the original clinical trials. DOHA stated that WAMTC reviews result in price decreases where there is strong statistical evidence that medicine sponsors have been paid at levels greater than justified by demonstrated health outcomes. Reviews have yielded \$500 million in savings to PBS expenses (DOHA, sub. DR71).

Keeping medicine prices low for users and containing the cost to taxpayers is the major focus of reforms to the PBS being implemented progressively from August 2007 (Abbott 2006). The Commission notes the views put forward by some participants that these reforms render WAMTC measures unnecessary. Questions about the continuing justification for WAMTC would need to be addressed by a separate policy review and are beyond the scope of this study.

Notwithstanding DOHA advice that ‘individual sponsors are able to quickly assess their situation using a WAMTC calculator and submit a suitable price response ...’ (DOHA, sub. DR71, p. 4), the costs of participating in WAMTC reviews claimed by pharmaceutical companies are substantial. While not all sponsors are obliged to obtain specific prescribing data additional to what is already subscribed for, or otherwise purchased, the cost of purchasing data is a particular concern.

According to Pfizer (sub. DR53), in order to establish prices under WAMTC for medicines where the price is above the PBS co-payment level, manufacturers have to purchase data on prescription volumes from Medicare Australia. In such cases Medicare Australia’s cost recovery fees form a large component of WAMTC compliance costs for firms. Given the rationale for the WAMTC policy and the Government’s broader health policy objectives, it may be appropriate to review whether charging for this data is consistent with the Australian Government’s Cost Recovery Guidelines. Consideration should also be given to whether there might be efficiencies if DOHA were to access the required data from Medicare Australia directly.

Consideration needs to be given either to modifications to the WAMTC reference pricing methodology or to adoption of an alternative methodology that would reduce the compliance burden on business and administration costs for PBPA, while not compromising the achievement of the Government’s objectives. Within the existing WAMTC methodology, options to consider might include reducing the frequency of reviews for any group of medicines, and accepting alternative data sets that are less costly to collect and analyse.

The Department of Health and Ageing should examine ways to reduce compliance costs for business associated with the Weighted Average Monthly Treatment Cost methodology for reference pricing, including by making better use of extant Medicare data, consistent with ensuring tax payers continue to get the best value from Pharmaceutical Benefits Scheme listed medicines.

Delays in achieving PBS listing due to overlapping processes

Medicines Australia (sub. 35), Johnson and Johnson Family of Companies (sub. DR70) and Pfizer (sub. 31) all raised concerns about the time taken from initial application to register a medicine with the TGA through to listing of the medicine on the PBS.

... we routinely spend around two years before a product is listed on the PBS and, in some cases, we may lose half the patent protected-period waiting for listing. (Pfizer, sub. 31, p. 4)

The average time it takes now from drug submission to when it comes on the PBS is between 24 and 30 months (Chairman Medicines Australia quoted in *Age* Newspaper, p. 3, 29 April, 2008)

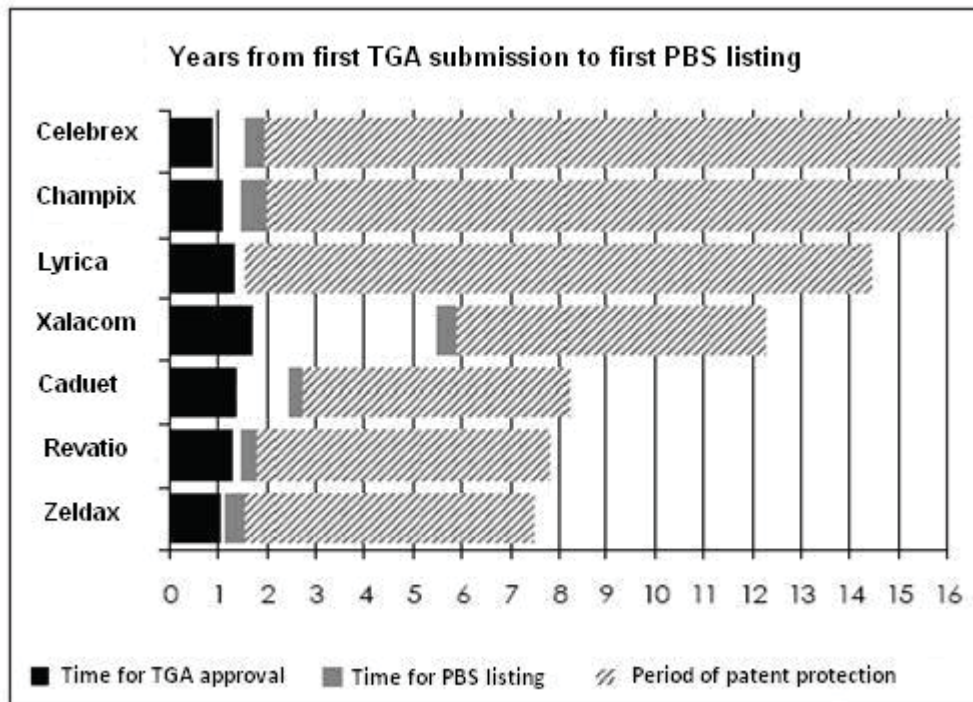
Figure 4.2 illustrates approval and assessment timeframes for a selection of Pfizer's recently-listed products.

Delays in getting medicines listed on the PBS have been attributed to overlap and duplication in some aspects of the TGA registration and PBAC/PBS listing processes and the lack of alignment or synchronisation of these processes.

Currently you put an application to the TGA and you wait between a year and a year and a half and then towards the end of the process you apply for PBS listing. (Chairman Medicines Australia quoted in *Age* Newspaper, p. 3, 29 April, 2008)

... the PBAC and TGA assessment periods are not synchronised at the moment, so efficiencies are fortunate rather than planned. For example, the date we receive approval from the TGA may be just after the cutoff for PBAC submissions (meaning we have to wait several months if we miss the cut-off date), and the TGA process itself may be delayed. (Pfizer, sub. 31, pp. 4 5)

Figure 4.2 Delays in achieving registration/PBS listing



Note: Lyrica was not listed on the PBS (although the PBAC recommended the product for listing the price was not commercially viable).

Data source: Pfizer (sub. 31, p. 4).

Assessment

As noted in section 4.1 above, currently the TGA assesses the quality, safety and efficacy of medicines in determining whether a medicine can be included on the ARTG and legally sold in Australia. TGA’s assessment does not consider the cost-effectiveness of medicines.

All pharmaceuticals must have TGA approval before they can be listed on the PBS. However, PBAC accepts submissions to have medicines listed before finalisation of ARTG approval, provided that the TGA delegate has recommended the medicine for registration in their overview. In practice, current processes allow PBAC to commence its assessment of a medicine when it is around two-thirds of the way through the TGA process. There is further flexibility in particular cases, allowing ‘assessments to commence earlier in the TGA process when a new medicine provides a real advance in the treatment or prevention of disease’. (DOHA, sub. DR71, p. 5)

The PBAC assessment is essentially about questions of cost-effectiveness and value for money for the tax payer. The PBAC accepts that products included on the ARTG have established adequate safety and efficacy to allow marketing in Australia. However, as noted by Medicines Australia, ‘companies are required to provide evidence of efficacy and safety as well as cost-effectiveness’ in their submissions to PBAC (sub. 35, p. 6) thus overlapping to some extent with the information submitted to TGA.

The pharmaceutical medicines industry has called for manufacturers to be able to make synchronised/parallel applications to the TGA and the PBAC. It has been suggested that this could reduce the total time to PBS listing by some six months.

Each organisation is concerned with different assessment questions – the TGA with effectiveness and safety; the PBAC with cost effectiveness – so at a level of principle, there is little to impede the two evaluations happening in parallel. (Pfizer, sub. 31, p. 4)

These issues are currently being examined by the joint Medicines Australia/DOHA Access to Medicines Working Group (AMWG), established as a result of reforms to the PBS announced in November 2006.

The AMWG has been considering the capacity for better streamlining and coordination of TGA/PBAC processes with a view to achieving improved efficiency and more timely processes. Under its terms of reference, the AMWG is charged with exploring the capacity to further streamline and coordinate regulatory approval, reimbursement and pricing processes to reduce the time it takes to list a medicine on the PBS. AMWG met with representatives of the PBAC, the TGA, consumers and the generic medicines industry to discuss these issues. The AMWG recently delivered its Interim Report to Government and it is under consideration.

There is also currently an investigation of ways to streamline medicine safety evaluation of applications for registration and reduce time to registration and subsequent PBS listing being undertaken by TGA internally.

While there would appear to be considerable merit in greater streamlining of assessments by TGA and PBAC, in principle there may also be some potential for inefficiencies or unnecessary effort, including some risk of wasteful diversion of scarce medicine assessment resources, in a system of parallel assessments. DOHA submitted that the most significant risk is that the subsidy recommendation by PBAC is not aligned with the TGA approved uses of the product:

Further streamlining current TGA and PBAC processes is not without risk. ... As medicines cannot be subsidised for non-approved uses, PBAC may need to reassess its recommendations which would result in significant delays in achieving PBS listing and additional costs to both Government and industry. (DOHA, sub. DR71, p. 5)

Medicines Australia (sub. DR64), Johnson and Johnson Family of Companies (sub. DR70) and Pfizer (sub. DR53) expressed the view that significant additional costs to Government were unlikely. Medicines Australia stated:

... most submissions to TGA are approved and there is no major reason why any changes to indication as a result of TGA evaluation (which are not common) could not be incorporated into an already-commenced PBAC evaluation. (sub. DR64, p. 3)

Consideration might be given to a system whereby companies are given the option to request parallel processing, rather than it being the default. The Commission acknowledges that the existing costs associated with seeking PBS listing already provide an incentive for firms to avoid the pursuit of unlikely listings. With cost recovery for PBAC services announced in the May 2008 Budget industry would have a further incentive to ensure requests for parallel processing would only be made when there was a high level of confidence that it would not result in significant inefficiencies, or unnecessary effort and cost.

RESPONSE 4.3

The Pharmaceutical Benefits Advisory Committee should be allowed, when requested by applicants, to conduct its assessment of a medicine for Pharmaceutical Benefits Scheme listing in parallel with the Therapeutic Goods Administration's assessment of the application to register the medicine.

One other issue that impacts on timeframes for PBS listing relates to the requirement for higher cost medicines to be approved by Cabinet before they can be listed. Since 2002, medicines expected to cost more than \$10 million a year in any of the first four years must be considered by Cabinet. The Commission understands that this requirement can add up to four months to the process compared to medicines that do not require Cabinet approval. The \$10 million threshold has not been indexed and will be triggered more often as the cost of medicines increases. The Government should consider the merits of increasing the threshold to account for price changes over the past six years and implementing an automatic annual indexation adjustment.

Concerns about marketing and advertising rules

In relation to the area of marketing and advertising restrictions, participants raised the following specific concerns:

- regulations governing the advertising of medicines are confusing and the majority of pharmacists and the public are not aware of how the associated advertising complaints system, which differs across jurisdictions, works. (Pharmacy Guild, sub. 15, p. 8)

-
- requirements, imposed by the Australian Competition Tribunal, on Medicines Australia member companies to disclose details of all educational meetings and symposia this ‘reporting and disclosure process imposes considerable administrative and financial burden upon companies with the cost of compliance for the industry in the millions of dollars’ (Medicines Australia, sub. 35, pp. 8-9). Further, because the requirements imposed under the Code apply only to Medicines Australia members, they place an excess compliance burden on members over and above other (non member) suppliers of prescription medicines (Medicines Australia, sub. DR64, and similar concerns were raised by Johnson & Johnson Family of Companies, sub. DR70).
 - the Fourth Community Pharmacy Agreement imposes obligations and offers incentives (to wholesalers) which disadvantage manufacturers that wish to distribute products directly to pharmacies.

Assessment

Concerns about regulations governing the advertising of medicines and the associated complaints system were raised with the Regulation Taskforce (2006), which recognised the need for reform:

The Australian Government should simplify the regulatory system for advertising therapeutic products to provide greater clarity and awareness of pharmacies’ obligations. (recommendation 4.16)

The Government agreed to this recommendation and a new regulatory model for advertising therapeutic products was being developed in preparation for the proposed Australia New Zealand Therapeutic Products Authority (ANZTPA). Draft regulatory instruments had been prepared and extensive stakeholder consultation undertaken.¹²

In July 2007, the New Zealand Government announced that New Zealand would not be ‘proceeding at this stage with legislation that would have enabled the establishment of a joint agency with Australia to regulate therapeutic products.’¹³

In the draft report the Commission suggested that the Australian Government should implement the proposed ANZTPA reforms to streamline and clarify advertising rules in an Australian-only context. In commenting on the draft report, the Complementary Healthcare Council of Australia opposed this, submitting:

¹² Such as the Australia New Zealand Therapeutic Products Regulatory Scheme (Advertising) Rule 2006.

¹³ ANZTPA website, <http://www.anztpa.org> accessed April 2008.

... the ANZTPA model can no longer be regarded a suitable model as considerable time has elapsed (4-5 years) since it was developed and there was also considerable industry concern expressed about the proposed model at the time. (sub. DR68, p. 4)

In light of such outstanding concerns, further consideration should be given as to how best to streamline and clarify advertising rules, including the most appropriate requirements for complementary medicines. The Commission understands that the TGA is consulting with stakeholders on the proposed ANZTPA reforms so that they can move forward in an Australia-only context. This includes possible changes to the advertising regulatory arrangements which would streamline requirements and simplify the complaints system. Specific consideration is being given to implementing a centralised mailbox for all complaints about therapeutic goods advertisements (DOHA, sub. DR71).

It is important that this consultation process takes account of the concerns of industry groups such as the Complementary Healthcare Council of Australia and that alternative models are actively considered.

RESPONSE 4.4

After further consideration of the most appropriate model, the Australian Government should streamline and clarify advertising rules and work with state and territory governments to ensure reforms also address the need for a simplified system for complaints about national advertising.

Regarding information disclosure requirements, all Medicines Australia members are required to make public disclosure every six months of all educational meetings and symposia held or sponsored by the company.

The Australian Competition Tribunal (the Tribunal) imposed these requirements as a condition of its authorisation, in June 2007, of the 15th Edition of the Medicines Australia Code of Conduct. Authorisation exempts Medicines Australia members from anti-competitive conduct provisions of the Trade Practices Act which might otherwise be breached by implementation of the Code.¹⁴

Failure to comply with the reporting requirements will constitute a breach of the Medicines Australia Code, resulting in probable adverse findings from the Code Committee followed by sanctions.

¹⁴ The Australian Competition and Consumer Commission (ACCC) had granted conditional authorisation of the Code of Conduct in July 2006, but Medicines Australia subsequently sought a review of this decision by the Tribunal.

Information that member companies must report includes details of venue, duration, attendees, nature and total cost of hospitality provided and total cost of the function. Medicines Australia is required to publish the information on its website and to conduct reviews of the information.

These requirements are intended to minimise the possibility of non-arms length relationships between pharmaceutical companies and health care professionals (and the receipt of direct benefits from companies) influencing prescribing practices, such that patient care might be compromised.

Although the Code seeks to impose some control, the Tribunal considered it to be insufficient and that public disclosure and the associated public scrutiny would provide a stronger incentive for appropriate self-imposed restraint by companies. The Tribunal, in its decision, considered that the disclosure conditions:

... increase the likelihood that the public benefit claimed for the Code is realised in respect of the provisions dealing with the conferral of such benefits on doctors. (Application by Medicines Australia Inc [2007] ACompT4, paragraph 8, as quoted in ACCC, sub. DR55, p. 2)

The Tribunal did give some consideration to the likely compliance costs associated with the disclosure requirements, but did ‘not consider that such burdens are unreasonable having regard to the benefit likely to be derived from the condition’ (Application by Medicines Australia Inc [2007] ACompT4, paragraph 363, as quoted in ACCC, sub. DR55, p. 2).

While the objectives for these quasi-regulatory disclosure requirements are clear enough, it is apparent from the concerns of participants that the compliance costs are substantial and may be greater than was anticipated by the Tribunal.

The ACCC advised (sub. DR 55) that because the current authorisation of Medicines Australia’s Code has been granted by the Tribunal, it is not able to vary or amend the authorisation (and its disclosure conditions). It would be up to Medicines Australia to seek authorisation for its Code once the current Tribunal authorisation expires, or for any new or amended Code, if it wishes to retain the protection provided by authorisation. At such time there would need to be careful consideration of any disclosure requirements to ensure that the specific details that must be disclosed, reporting formats and frequency of reporting, impose the minimum compliance burden consistent with achieving the public scrutiny objectives of the requirements.

The Commission does not support the suggestion made by Medicines Australia (DR64) and Johnson & Johnson Family of Companies (DR70) that the disclosure requirements and other provisions of the Medicines Australia Code should apply to

non-member companies as well and be a condition of marketing approval. The Commission notes that:

- the disclosure requirements were only imposed by the Tribunal as a condition of authorisation of the Code, which otherwise may have been in breach of provisions of the Trade Practices Act
- membership of Medicines Australia is purely voluntary and as with any such industry association a decision to apply for membership or to maintain membership is based on an implicit weighing up of the benefits (advantages) of membership against any costs (disadvantages).

In the Fourth Community Pharmacy Agreement, the margins that wholesalers may charge for PBS products in sales to pharmacies was reduced and a Community Service Obligation (CSO) was introduced. The CSO imposed certain key restrictions and service delivery expectations on suppliers to ensure universal patient access, including:

- a requirement to supply all medicines on the PBS within 24 hours of a pharmacy placing an order in most areas of Australia
- being able to supply the full range of PBS products, with set criteria on lower volume products.

In return, eligible wholesalers are entitled to claim a government subsidy. Claims are submitted on a monthly basis and are based on sales volume and composition. Currently only wholesalers may claim the subsidy.

Pfizer's concern is that the CSO incentive scheme provides a competitive advantage for eligible wholesalers (receipt of government funding can allow them to sell to pharmacies at lower prices) and creates disincentives for pharmaceutical companies to supply direct to pharmacies. Pfizer claim that the subsidy scheme prevents competition and contributes to over-servicing and other distribution inefficiencies. They have suggested that a parallel scheme should be available to manufacturers supplying direct to pharmacies under the same CSO 'with the single distinction that they are only obliged to stock all of their own medicines (not the full PBS list)' (Pfizer, sub. 31, p. 12).

The intention of the CSO incentive scheme is to ensure universal patient access to PBS products. The government funds paid to wholesalers are the *quid pro quo* for cost inefficiencies that the suppliers bear in order to meet restrictions imposed, for example having to hold more stock, including low volume products, and to have in place more costly distribution arrangements that guarantee prompt supply.

The concerns raised by Pfizer and the merits of its proposal to broaden the Community Service Obligation incentive scheme fall outside the terms of reference for this review because they relate to the policy underpinning the scheme.

Concerns regarding supply of PBS medicines

The Pharmacy Guild of Australia raised the following concerns in relation to the supply of PBS medicines:

- the ‘Safety Net 20 day rule’ is considered to be ‘unworkable and impractical for pharmacists and unfair and potentially a health risk for patients’ (Pharmacy Guild, sub. 15, p. 5).
- problems with PBS supply arrangements in the context of aged care residential facilities and private hospitals – such as dealing with a prescription for less than one month’s supply of medication when an aged care facility may require the pharmacy to provide one or even two month’s supply. The pharmacist ‘is forced to “bend the rules” and supply medication on an “owing script” basis’ and then bear the burden of following up with the doctor to obtain a written prescription so that the resident can receive medicines at the subsidised PBS price. These problems are causing ‘enormous frustration and time wastage by ... nurse[s], doctors and pharmacists involved in the administrative process of supplying medicines ...’ (Pharmacy Guild, sub. 15, pp. 6–7).

Neither is a new concern, both having been raised with the Regulation Taskforce.

Assessment

Under the PBS Safety Net, once heavy users of medicines reach a certain safety net threshold in a calendar year, they can apply for a PBS Safety Net Concession (CN) card, which enables them to access PBS medicines free or at a much reduced cost for the remainder of the calendar year.

These Safety Net entitlements can act as an incentive for repeat prescriptions to be used to obtain medicines earlier than they are needed. The Safety Net ‘20 day rule’ was introduced to discourage hoarding and wastage of medicines by requiring a 20 day gap between separate dispensing of certain specified PBS medicine. A resupply within 20 days falls outside Safety Net benefits and any patient contribution does not count towards the Safety Net threshold. If the Safety Net threshold has been reached, the usual patient co-payment applies, rather than the free or reduced Safety Net amount.

Repeats may be necessary within the 20 day period, ‘where, for example, the doctor requires the medicine to be taken more frequently than normal, where the patient loses the prescription, or where the patient is travelling and has left their medicine behind’ (Pharmacy Guild, submission to Regulation Taskforce, quoted in sub. 15, p. 5). The Pharmacy Guild has also highlighted particular difficulties implementing the 20 day rule in nursing homes (especially with respect to maintenance of supply and packing more than one month supply in a dose administration aid) and in rural and remote locations (a patient may only be able to access pharmacies on infrequent visits to town).

The Commission notes that the ‘Safety Net 20 day rule’ applies to only certain PBS medicines prescribed for long-term therapy. Importantly:

- it does not apply to any medicines for acute conditions or short-term use
- if an additional or early supply of a medicine to which the rule applies is genuinely needed, a PBS-subsidised supply can still be obtained.

DOHA provided the following comments:

It is reasonable that extra supplies are charged at a person’s usual co-payment, as this amount already takes into account the person’s ability to pay. As many PBS medicines are expensive, the benefit of being able to access an early PBS-subsidised supply at the usual co-payment rate outweighs the Safety Net effects. (pers. comm., 5 June 2008)

The Regulation Taskforce (2006) recommended that ‘The Australian Government, in consultation with pharmacies, should review the impact of changes to the 20 day rule, to address negative impacts on pharmacies and consumers’ (recommendation 4.13).

In its response, the Australian Government did not agree to this recommendation:

The Australian Government introduced the 20 day rule as a budget measure which is expected to save \$70.1 million over four years. The rule supports good practice in the safe use of medicines by discouraging patients from obtaining additional, or early, supplies of medicines. The Australian Government has worked with the pharmacy sector to provide explanatory materials to ensure that the new arrangements are implemented in an efficient manner and are understood by patients and pharmacists. The Australian Government will continue to work with the sector to ensure that policies aimed at quality use of medicines are implemented effectively. (Australian Government 2006, p. 7)

It is clear, therefore, that the change to the 20 day rule was a deliberate policy decision designed to reduce the budgetary cost of the PBS and also to address safety concerns associated with hoarding of medicines. Therefore the issue falls outside this review’s terms of reference. DOHA’s present view is that the policy objectives are being met:

While there were some initial concerns raised regarding the introduction of the Safety Net 20 day rule in January 2006, no compelling arguments have been identified that suggest the need to change, or review, the application of the rule. This policy appears to have been effective in helping to contain PBS outlays, while at the same time supporting good practices for safe use of medicines in the community. (pers. comm., 5 June 2008)

Notwithstanding this view, now that the revised arrangements have been in operation for more than two years, the operation of the 20 day rule could be evaluated to verify the actual savings that have been achieved compared with any costs imposed on consumers, pharmacists or others.

With respect to concerns about the supply of PBS medicines in aged care residences and private hospitals, the Regulation Taskforce (2006) recommended that:

The Australian Government should review the supply of PBS medicines in residential aged care facilities, including what may constitute a prescription in this setting, and safe and effective packaging issues' (recommendation 4.15)

The Australian Government agreed in principle to the recommendation:

The intent of this recommendation is consistent with and addresses Part 6, Section 38.1 of the Fourth Community Pharmacy Agreement, which commenced on 1 December 2005. This states that "the parties agree to undertake a review of the existing PBS supply arrangements in the context of aged care residential facilities and private hospitals". The precise scope of this review is currently being considered. The review will be completed by 30 November 2006. (Australian Government 2006, p. 7)

The Commission notes that this review has only recently commenced. The commencement of the Review was delayed at the request of the Pharmacy Guild of Australia pending finalisation of the PBS Reforms negotiations.

The Review is being overseen by the Pharmacy Guild and DOHA, as the parties to the Fourth Community Pharmacy Agreement, and facilitated by an independent consultant, Healthcare Management Advisors. The Review is to consider changes to relevant legislation that would improve the efficiency and effectiveness of PBS supply (including through community pharmacies) to aged care residential facilities and private hospitals and possible alternative models of PBS supply to such facilities. The Review is expected to conclude in late 2008 (DOHA, pers. comm., 12 June 2008).

Other concerns

Various concerns were raised by Medicines Australia and Pfizer in relation to aspects of Australia's intellectual property (IP) regime, in particular issues

surrounding the enforcement of patent rights and inadequate data exclusivity periods. In relation to patent rights, a specific concern related to changes introduced during the passage of legislation to implement the Australia-United States free trade agreement in 2004, which introduced patent certification requirements that Pfizer (sub. 31) described as ‘unworkable’ (p. 3) and ‘administratively burdensome’ (p. 13).

These amendments [the so called ‘Latham amendments’] facilitate early market entry by generics before patent expiry without prior notice to the patent holder, and actively deter patent holders from defending their patents ... (Medicines Australia, sub. 35, p. 9)

The Commission acknowledges that the operation of these amendments could create a significant burden for patent holders, particularly through:

... increased patent litigation costs for the originator pharmaceutical industry. Companies are increasingly forced to defend more valid patents against infringements than in the past ...

... [A]n increase in unnecessary litigation ... increases red tape and cost of doing business in Australia. Moreover, due to a lack of sufficient notification to innovator companies of ... an impending entry of a generic competitor brand, originator companies are compelled to spend considerable time, money, and resources to keep track of whether generic companies are intending to seek marketing approval for patented medicines. (Medicines Australia, sub. DR 64, p. 5)

However, the Commission considers that these burdens are intrinsically tied to the pursuit of the policy objective, namely to facilitate early market entry for generic medicines. As such, in accordance with the terms of reference for this review, these intellectual property issues have not been assessed by the Commission as part of this report. They should be considered in the context of the Review of the National Innovation System, currently being conducted by an expert panel, chaired by Dr. Terry Cutler, which has as part of its terms of reference to ‘identify regulatory barriers to innovation and recommend ways to minimise these’. The Commission notes that both Medicines Australia and Pfizer have made a separate submission to that Review raising the concerns identified above and other issues relating to the protection of intellectual property.

In conducting the Review, the Panel is to have regard to relevant reports and studies, including the Productivity Commission’s Report on Public Support for Science and Innovation (PC 2007c). A ‘Green Paper’ detailing policy options is to be provided to the Government by the end of August 2008 and will be used as the basis for the development of a Government ‘White Paper’ to be delivered by the end of the year.

4.3 Overview of medical devices regulation

Medical devices are products used in the diagnosis, prevention, treatment and management of disease and disability. They range from more basic or everyday items such as medical gloves, bandages, syringes, condoms and disinfectants through to high technology items such as in vitro diagnostic devices, X-ray equipment, surgical lasers, orthopaedic implants, cardiac defibrillators and pacemakers, and dialysis equipment.¹⁵

Medical devices are regulated under the Therapeutic Goods Act. The Act was amended in 2002 to introduce a new system for medical device regulation incorporating the principles of the international regulatory model developed by the Global Harmonization Task Force (GHTF).¹⁶

Assessing safety and performance and approval for sale

The TGA conducts three key assessment processes for medical devices:

- conformity assessment procedures that assess requirements imposed on manufacturers
- assessment of applications for inclusion of devices on the ARTG¹⁷
- post-market monitoring, surveillance and review of medical devices.

Medical devices cannot be marketed in Australia unless they are approved by the TGA for inclusion on the ARTG or are specifically exempt in the legislation. The TGA uses a risk-based approach to assess the safety and performance of devices, against essential principles defined in the Act. The essential principles set out the requirements relating to the safety and performance characteristics of medical

¹⁵ The term ‘medical technologies’ is sometimes used as an alternative to or interchangeably with ‘medical devices’. Whilst not a clearly defined term, the Commission considers that ‘technologies’ is a broader term than devices. Generally in this section the term devices is used when discussing the regulatory framework since this term is defined in Section 41BD of the Therapeutic Goods Act and this determines the scope (product coverage) of the Act.

¹⁶ Australia’s regulatory model is aligned with the GHTF model rather than the European model. Although the GHTF has its origins in the European process, there are some important differences between the European and GHTF models. With recent reviews of the relevant Directives in Europe, technical requirements are now more closely aligned, but differences in implementation remain.

¹⁷ A small number of applications are also assessed by the Medical Devices Evaluation Committee (MDEC), comprising expert clinicians. The MDEC provides advice to the Minister for Health and Ageing and the TGA on safety, quality, performance and timely availability of medical devices.

devices. The principles may define results to be achieved, performance levels, hazards to be addressed or issues to be considered, but do not necessarily specify how they must be satisfied or complied with. Thus, compliance with applicable medical device standards is not required, but is one way to establish compliance with the essential principles. This provides greater flexibility for manufacturers and scope to adapt more readily to technological advances or changes in the application of medical devices.

Medical devices are classified to one of five categories according to classification rules based on the risk presented to the patient, the user and the environment (see table 4.1).

Conformity assessment must be performed before a device can be included in the ARTG. Conformity assessment is the manufacturer's responsibility, and requires the manufacturer to certify that the medical device conforms to the essential principles of safety and performance and that an appropriate conformity assessment procedure has been applied. Supporting technical documentation is required. For low risk (Class I devices – eg non-sterile gloves and gowns, elasticised bandages, etc) manufacturers self certify and there is no pre-market audit.

The TGA, or an overseas 'Notified Body', issues certification after confirming the Conformity Assessment procedures applied by the manufacturer are appropriate. Assessment by the TGA is required for Australian manufacturers of medical devices intended for supply in Australia. The decision to issue a conformity assessment certificate depends on several factors, including: the application of quality management systems; certification of compliance with the essential principles; and that the applicant and relevant other people within the manufacturer's organisation are fit and proper persons within the meaning of the regulatory framework.

Lower risk category devices are usually included in the ARTG automatically once a proper application is made, together with the appropriate certification. Applications may be selected by TGA for an Application Audit which involves checking some or all aspects of the application and certification. Applications for inclusion of medical devices onto the ARTG can be submitted electronically using the Device Electronic Application Lodgement (DEAL) System. Applications for both registration and listing on the ARTG for certain other therapeutic goods, but not pharmaceutical medicines, can also be lodged through DEAL.

Overseas manufacturers can either arrange for the TGA to undertake the necessary assessments or present evidence of acceptable assessment to the appropriate European Medical Devices Directive, and supplement this with the preparation and signing of a Declaration of Conformity to Australian requirements.

For over 97 per cent of medical devices, that evidence is provided in the form of either an EC Certificate issued by one of the 78 Notified Bodies operating in Europe, or an MRA Certificate issued by one of the 18 Conformity Assessment Bodies approved for the purposes of the Australia-European Mutual Recognition Agreement. (TGA pers. comm., 11 August 2008)

Transitional arrangements for the implementation of the new regulatory system included a two year transition period (until October 2004) for all devices that met the definition of a medical device, but were previously exempt from entry on the ARTG or were excluded under the Therapeutic Goods (Excluded Goods) Order of 1998. A five year transition period was allowed for medical devices registered or listed in the ARTG prior to October 2002 to be included in the ARTG under the new system.

Assessment for funding/reimbursement

The Medical Services Advisory Committee (MSAC) makes recommendations to the Minister about public funding of *professional services* involving medical technologies and procedures, most commonly via the Medicare Benefits Schedule. MSAC assesses the safety, clinical effectiveness and cost effectiveness of medical technologies and procedures in response to submissions from the industry or references from government.

MSAC funds and organises assessments, but the majority are undertaken by contracted evaluators, overseen by an expert advisory panel chaired by a member of MSAC. MSAC members are appointed by the Minister and include: specialist practitioners; general practitioners; health economists; a health consumer representative; health planning and administration experts and epidemiologists.

The Prostheses and Devices Committee (PDC) makes recommendations to the Minister on the listing and benefit levels of new prostheses on the Prostheses List¹⁸ which, under the *Private Health Insurance Act 2007*, determines those items that private health insurers are required to reimburse. The PDC does not consider, or make recommendations about, public funding.

Private health insurers are required to pay benefits for a range of prostheses that are provided as part of an episode of hospital treatment or hospital substitute treatment where the patient is covered for the treatment. The legislation does not define

¹⁸ Prostheses on the List include cardiac pacemakers and defibrillators, cardiac stents, hip and knee replacements and intraocular lenses, as well as human tissues such as human heart valves, corneas, bones (part and whole) and muscle tissue. The list does not include external legs, external breast prostheses, wigs and other such devices.

‘prosthesis’, however, the Minister has endorsed a set of criteria for listing products on the Prostheses List.

The PDC considers the safety and clinical effectiveness of prostheses. It does not formally consider cost effectiveness, but does provide advice on appropriate benefits that have been negotiated between the Prostheses and Devices Negotiating Group and the sponsors. PDC members include: clinicians; insurers; private hospital nominees and representatives of consumer groups and the medical technology industry.

All medical devices to which the TGA legislation applies must be included on the ARTG before an application can be made for assessment by the Medical Services Advisory Committee or Prostheses and Devices Committee (if appropriate).

4.4 Concerns about medical devices regulation

Concerns were raised about various aspects of the regulatory arrangements for medical devices. These are discussed under the following headings:

- TGA monopoly on conformity assessment for Australian manufacturers
- timeliness, transparency and consistency of assessments/approvals
- definition of the central circulatory system
- problems associated with access to funding and reimbursement
- multiple and overlapping processes.

Most of the concerns are not new and have been raised in submissions to various reviews, including: a DOHA administrative review of the Medical Services Advisory Committee (2004-5); the Commission’s Research Study on Impacts of Advances in Medical Technology (PC 2005b); the Regulation Taskforce (2006); during the development of the Medical Devices Industry Action Agenda (DITR 2006); and the recent Doyle Review of Prostheses Listing (2007).

The Medical Technology Association of Australia (MTAA) are concerned about slow progress, submitting that the industry ‘has seen little progress in structural reform to processes ... [if] anything MTAA has seen additional impositions on industry ... as a result of failures to restructure and address the inconsistencies and inequities in access to medical technologies’ (sub. 23, pp. 5-6).

TGA monopoly on conformity assessment for Australian manufacturers

Under the Therapeutic Goods Act, the TGA is required to examine and certify the conformity assessment procedures undertaken by Australian manufacturers. While the Act permits the TGA to accept CE certification for medical devices manufactured overseas, it mandates inspections by the TGA for Australian manufacturers of equivalent devices.

The MTAA (sub. 23) claim that this disadvantages Australian manufacturers relative to their direct competitors overseas in terms of the costs of the domestic inspections and time delays. In its submission to the Regulation Taskforce, the Medical Industry Association of Australia (MIAA, as the MTAA was named at that time) provided an indication of the magnitude of the regulatory cost disadvantage faced by Australian manufacturers of medical devices:

... it is 36 times more difficult for this company to recover regulatory costs from sales in Australia than in Europe. This situation is created by compulsory TGA inspections, the associated fees and the small size of the market.

Initial costs for these inspections typically range from approximately \$20 000 to \$200 000 (if the device contains an unapproved medicinal component) with costs of \$6 000 for regular surveillance audits every 12 to 20 months. (MIAA 2005, p. 7)

Assessment

In addition to being considered by the Regulation Taskforce, the TGA's monopoly was discussed in the Productivity Commission's Research Study on Impacts of Advances in Medical Technology (PC 2005b) and the Medical Devices Industry Action Agenda (DITR 2006).

The Regulation Taskforce (2006) recommended:

The Australian Government should consider allowing Australian manufacturers to choose a certification body (acceptable to the Therapeutic Goods Administration), based in Australia or overseas, to verify and certify their conformity assessment procedures (having regard to the recommendations of the Medical Devices Industry Action Agenda). (recommendation 4.19)

The Government agreed to this recommendation and stated in its response that the issue, and best practice regulation for devices more generally, would be considered as part of the implementation phase for the Medical Device Industry Action Agenda (Australian Government 2006). However, the Government has concluded the Action Agenda process and the issue remains unresolved, so an alternative process

is needed for considering best practice regulation for devices and for introducing third-party conformity assessment.

The ability of Australian manufacturers to use a certification body other than the TGA, was also raised as part of the stakeholder consultations during the development process for the Australia New Zealand Therapeutic Products Authority (ANZTPA). This and other issues identified during that process are now being discussed with the industry with a view to bringing these elements in to the Australian regulatory framework. DOHA submitted:

The TGA has conducted initial consultations with stakeholders on a possible model to enable the use of external assessment bodies in conformity assessment. Further consultations will be required acknowledging changing international experience. (DOHA, sub. DR71, p. 6)

Notwithstanding these recent developments, this issue has taken too long to resolve. The Regulation Taskforce recommendation to allow third party conformity assessment for Australian manufacturers should be implemented as soon as possible. A high priority should be given to resolving implementation details following the completion of the current consultation process.

RESPONSE 4.5

The Department of Health and Ageing should introduce amendments to the Therapeutic Goods Act 1989, and regulations as necessary, to allow Australian manufacturers to choose a certification body (acceptable to the Therapeutic Goods Administration), based in Australia or overseas, to verify and certify their conformity assessment procedures.

Timeliness, transparency and consistency of assessments/approvals

Concerns were raised about excessive timeframes for the processing of applications for registration of *higher risk* devices. MTAA, for example, stated:

Timeframes have extended for the processing of applications for registration of higher risk devices as a result of the backlog of applications ... arising from the surge of products transitioning to meet the cut-off date under the regulatory changes introduced in 2002 ... As a result there is a significant backlog in products awaiting conformity assessment (both new products caught up in the backlog) and transitioning products ... (MTAA, sub. 23, pp. 2 3)

Johnson & Johnson Family of Companies (sub. DR70) claimed that changes at the TGA aimed at clearing the backlog of re-registration applications are having a negative impact on evaluation times for new and innovative products while Medtronic (sub. DR62) submitted that generally timeframes for registration of

lower risk devices have become longer since the October 2007 transition cut-off date.

Medtronic (sub. DR62) also considers that the TGA is reporting inaccurately on its efficiency in meeting assessment timeframes, by ‘starting the clock’ from the date an officer is assigned, rather than when payment is received.

Several participants consider that there is insufficient recognition of overseas regulatory approval processes and assessments. For example:

Australia is in an excellent position to take greater advantage of regulatory approval processes undertaken by its international regulatory partners so that the emphasis of the regulatory resources in Australia can be changed to one of a structured post-market review process. (MTAA, sub. 23, p. 5)

In a market where over 90% of medical devices are imported and Australia represents less than 2% of the global medical device market it would be most effective for the TGA to focus on working with reputable overseas regulatory authorities and Notified Bodies to develop a common understanding of, and confidence in each other’s processes and decision making. (Johnson and Johnson Family of Companies, sub. DR70, p. 14)

[Medtronic has a concern] regarding ... [TGA] ... approval of medical devices containing components of animal origin or that contain substances classed as medicines. These applications are expensive and lengthy (approximately 18 months) and delay the entry of medical technology that may have already been assessed and approved by international notified bodies. (sub. 62, p. 3)

Medtronic (sub. DR62) and Johnson & Johnson Family of Companies (sub. DR70) also raised various concerns regarding transparency, communication and consistency in their dealings with TGA, including:

- a lack of transparency in conveying policy decisions and new application rules to industry
- a lack of accessibility of TGA officers
- inconsistency in decision making and advice
- a lack of clarity with regard to the reasons or justification for certain decisions.

Assessment

The life cycle of an average medical device is about 18 months. Medical devices are therefore less likely to benefit from extended patent protection and regulatory delays in getting products to the market place can be particularly costly.

Medical technology development has been characterised as a continuous, iterative process. This iterative and ongoing development process, characterised by constant

product changes made in response to user needs and preferences distinguishes medical technology innovation from other therapeutic products. ... systems which support speed to market are as critical to the survival and success of the industry as they are to the capacity to make new technologies available to patients who need them. (MTAA, sub. 23, p. 2)

The TGA reports publicly on its performance in meeting target timeframes for application processing.¹⁹ An analysis of information provided by the TGA for the latest available two quarters (July to December 2007) reveals that:

- for processing of DEAL applications, TGA's performance ranged from 98% completed within the target time of 15 days²⁰ for 'Manufacturing Evidence of Conformity Assessment' (where an overseas notified body has already issued certification) through to only 46% completed within the target time of 60 days for a 'Level 2 application audit' for an individual new device²¹
- for conformity assessment applications (where the TGA is required to issue certification, for example for Australian manufacturers), 76% of 'Schedule 3 Part 1' assessments were completed within the 90 day target time,²² 53% of 'Schedule 3 Part 1.6 Design Examination' assessments were completed within the 120 day target time²³ and all assessments were completed within the statutory time limit of 255 days.

The TGA received an extremely large number of applications for conformity assessment and inclusion onto the ARTG, for medical devices in the last year of the five year transition period to the new regulatory framework for medical devices, ending in October 2007.

The Therapeutic Goods Act has been amended to ensure that registered and listed medical devices transitioning to the new framework, for which an effective application was received before 4 October 2007, can continue to be supplied until their new application for inclusion is processed. New administrative processes have allowed the transitioning applications to be quarantined.

The TGA's priority is the processing of applications for new products and it has been focusing on meeting agreed industry/TGA timeframes for these applications. In relation to Medtronic's claims about inaccurate reporting by TGA on its timeliness, the Commission notes that the TGA's practice is to 'start the processing

¹⁹ See <http://www.tga.gov.au/about/tgabp0809.htm>.

²⁰ With an average completion time of 8 days and a range of 1 to 71 days.

²¹ With an average completion time of 73 days and a range of 1 to 269 days.

²² With an average completion time of 49 days and a range of 3 to 182 days.

²³ With an average completion time of 49 days and a range of 10 to 236 days.

clock' when the application becomes effective, that is when the application fee is received. The clock is stopped when the TGA is waiting for requested further information from the applicant or when further fees remain unpaid.

The processing of the transitioning applications is being managed separately and TGA is engaging the industry in a risk-based approach to prioritising the assessment of these applications and will report regularly on progress in clearing the backlog. The task of separating transitioning applications and prioritisation has been made difficult because not all sponsors clearly identified their applications as new or transitioning, and some applications include both types of product. The TGA has flagged that it is in the process of engaging additional resources to manage current workloads and the peak in applications received. (TGA, pers. comm., 28 April and 11 August 2008)

A review of business processes in the TGA, Office of Devices, Blood and Tissue was initiated in 2007. Consultation with industry has commenced on the Medical Device Business Improvement Program. The Business Improvement Program has a number of objectives, including to improve: efficiency in pre-market processing; transparency in decision making; industry understanding of the legislative framework; accuracy in the applications submitted; and more effective post-market monitoring of product safety.

Timeliness of approval processes is specifically being addressed as part of the Program. One significant measure will be the move to 'auto-inclusion' of all Class I medical devices onto the ARTG. The TGA is also working with the industry to address problems with the quality and completeness of the applications it receives, which has also contributed to delays in processing.

Also, as part of the Business Improvement Program, the TGA has recently implemented some initiatives which aim to provide stakeholders with more effective service, and these are likely to contribute to some improvement in transparency and consistency. This includes specific initiatives relating to written correspondence, telephone and email enquiries and website enhancements (including answers to 'frequently asked questions'). The TGA is also currently considering, across all program areas, ways in which the agency's decision-making processes can be made more transparent, including the publication of decisions (TGA pers. comm., 11 August 2008).

The Therapeutic Goods Administration (TGA) should ensure that the outcomes of its current Medical Devices Business Improvement Program include the implementation of measures to ensure improved transparency, consistency and timeliness in decision making, including provision of clear advice regarding the reasons for all decisions. The TGA should publish specific commitments and timelines for the Improvement Program.

Acceptance of overseas assessments

With respect to acceptance of overseas registrations/certifications, table 4.1 provides a summary of the assessment process for the different categories of devices. For lower risk devices the TGA currently accepts prior overseas registrations as part of its decision-making processes. Greater than 90 per cent of medical devices are entered on the Register without further assessment by the TGA

based on declarations by the manufacturer that the product is in compliance and where appropriate, supported by certifications issued demonstrating compliance with a regulatory framework similar to Australia. For higher risk devices, the application audit process is designed to ensure that devices have undergone the appropriate level of scrutiny, commensurate with the risks posed by their use.

Since adopting the principles of the Global Harmonisation Taskforce for the Australian regulatory framework for medical devices, the TGA has very similar data requirements to Europe and Canada. This makes preparation of the audit dossier simpler for the approximately eight per cent of applications which undergo the application audit process and are required to provide documentation to support an existing overseas certification.

Nevertheless, participants have concerns about the unnecessary cost and delays associated with what they perceive to be a duplicative process. Johnson and Johnson Family of Companies submitted:

In most cases, overseas manufacturers undertake the appropriate conformity assessment procedures for Class III devices by having Quality Management System certification issued by a Notified Body (NB) together with the preparation of a Design Dossier comprising technical product specific documentation for evaluation by the NB. ...

Rather than the audit process being a check that the appropriate conformity assessment process has been applied, the Level 2 Application Audit process is a duplicative evaluation process where much of the same documentation that was assessed by the NB in the Design Dossier review is re-evaluated by the TGA.

The overall cycle time for TGA approval for new products (not re-registrations) at present is approximately 6 months.

Since the TGA evaluation can only commence once the Design Dossier review has been completed and the Design Examination Certificate issued, the sequential nature of these two processes means that products are launched in Australia 6–9 months later than they are available in Europe. With the average lifecycle of a medical device being 18 months, the duplicated process conducted in Australia means that, not only are new technologies not available to Australian patients until much later than European patients but one third of the investment recovery period is lost. (sub. DR70, pp. 14-15)

The Australia-EU Mutual Recognition Agreement does provide a rapid path to TGA approval for Class III devices where the manufacturer is located in the EU and the device is substantially manufactured within the EU. Class III devices that have been reviewed and CE marked by a Notified Body can have a Mutual Recognition Agreement (MRA) Certificate issued, which is lodged with TGA and the product approved without any additional evaluation within two weeks. Johnson and Johnson Family of Companies called for an equivalent MRA process to be established with the US:

Class III devices from US manufacturers go through the identical process of Design Dossier review by a NB [Notified Body] however are then required to go through an additional costly 6 months review process by TGA in order to be included in the Australian Register of Therapeutic Goods (ARTG). (sub. DR70, p. 16)

The TGA has informed the Commission that it has commenced discussions with the US Food and Drug Administration in relation to mutual acceptance of device assessments (TGA, pers. comm., 11 August 2008).

More generally, Johnson and Johnson Family of Companies queried the need for TGA to conduct expensive overseas audits of manufacturers in non-EU member countries, where the facilities ‘are regularly audited by a reputable ... [Notified Body of the EU] ... with their audit reports and recommendations available for review by TGA ...’ (sub. DR70, p. 16).

There would appear to be scope for wider recognition by the TGA of prior overseas assessments for devices. A policy of generally accepting assessments from competent bodies that have demonstrated suitably rigorous assessment processes could potentially:

- reduce regulatory burdens for business
- reduce TGA administration costs and free up regulatory resources to focus on post-market monitoring and on pre market assessments for the highest risk devices
- facilitate quicker market access to new devices with consequent health benefits.

Table 4.1 Assessment procedures by category of device

| <i>Class of device</i> | <i>Proportion of medical device entries on ARTG^a</i> | <i>Assessment procedure</i> |
|---|---|--|
| Class I (low risk) | 58 | Not required to be assessed, either by an EU Notified Body for EU market entry or by the TGA for Australian market entry, but are entered on the Australian Register of Therapeutic Goods (ARTG) on the basis of the manufacturer drawing up an appropriate Declaration of Conformity certifying the products are in compliance with the regulatory framework. |
| Class IIa (low to moderate risk) | 22 | Class IIa (and all but four types of Class IIb) medical devices are entered on the ARTG supported only by evidence provided by the manufacturer that they, and the devices as appropriate, have been assessed and found in compliance with the EU regulatory framework for medical devices. It is expected the manufacturer will have drawn up and signed the appropriate Declaration of Conformity to support placing the device(s) on the Australian market, but this declaration is not required to be presented to the TGA. |
| Class IIb (moderate to higher risk — includes most implantable devices) | 15 | With the exception of four types of Class IIb devices, procedure is as for IIa. For the other four see procedure for higher risk devices. |
| Class III (high risk) | 4 | Of the remaining (approximately 10% of total entries on ARTG). |
| Class AIMD (high risk — implantable devices equipped with an energy source) | 1 | <ul style="list-style-type: none"> • 2 % of total entries are those devices required, by the Act, to have their conformity assessment processes reviewed by the TGA. This category includes devices from Australian manufacturers. • 8 %, which represent the highest risk devices, undergo an application audit — a desktop review process where certification(s) demonstrating compliance with a regulatory framework similar to Australia and documentation prepared by the manufacturer, or the assessment body, as part of the process to achieve that certification, is reviewed by the TGA. |

^a Devices available on the Australian market today, as represented by entries on the ARTG.

Source: Based on information provided by the TGA (per. comm., 11 August 2008).

However, for such a policy to ensure continuing high standards of devices available in Australia and deliver net benefits for the community, the TGA must have a high

level of assurance as to the quality of the assessments by the overseas bodies. The Commission notes the advice of the TGA (pers. comm., 11 August 2008) that its experience over recent years, including in reviewing documentation supplied as part of the application audit process, has revealed:

- some variability in the competence of Notified Bodies of the EU to assess high risk devices and variability in the standard of clinical evidence collection and evaluation
- evidence of different manufacturing standards being applied to a product sourced from the same overseas manufacturer, depending on the ultimate destination market.

Similar concerns have been identified by European authorities. The EU is currently considering a complete restructure of the Medical Device Directives, including a ‘drawing back’ of assessment of high risk devices to a centralised assessment body, akin to the European Medicines Evaluation Agency, and away from the various Notified Bodies.²⁴

RESPONSE 4.7

The Therapeutic Goods Administration (TGA) should examine the scope to make greater use of acceptable prior overseas assessments. This should include identifying competent inspection bodies overseas. In general, where a device has been approved by such bodies there should be no requirement for a further assessment by the TGA.

Definition of the central circulatory system

Johnson & Johnson Family of Companies (sub. DR70) submitted that differences between the Australian and European definition of the central circulatory system results in classification of some devices to the higher risk Class III in Australia compared to Class IIb in Europe, with corresponding increases in compliance costs. In order to complete the appropriate conformity assessment procedure as a Class III device specifically for Australia, the manufacturer is required to undertake ‘a great deal of additional work to prepare a Design Dossier for the product and submit it to the NB [Notified Body] for evaluation in order to have a Design Examination Certificate and Summary Technical Report issued’ (Johnson & Johnson, sub. DR70, p. 17).

²⁴ See *Public Consultation on a Recast of the Medical Devices Directives* available at (http://ec.europa.eu/enterprise/medical_devices/consult_recast_2008_en.htm), accessed 14 August 2008.

Assessment

Concerns about inconsistencies in the definition of the central circulatory system were raised with the Regulation Taskforce (2006), which recommended the Australian Government should apply an internationally agreed definition of the central circulatory system to all applicable medical devices. (Recommendation 4.20)

The Government agreed to this recommendation and has worked closely over recent years with its international counterparts to harmonise with an internationally-accepted definition of the central circulatory system. However, around the world there are differing views on the most appropriate definition. Australia although not aligned with the European definition, is aligned with the internationally accepted definition as set out by the Global Harmonisation Taskforce (GHTF). The Commission notes that member economies of the Association of South East Asian Nations (ASEAN) and the Asian Harmonisation Working Party (AHWP) are working to introduce the GHTF regulatory framework and hence their definitions will also align with the principles of the GHTF.

In the longer term, achieving alignment between the GHTF and European Medical Devices Directives should be the goal for regulators internationally. This would facilitate trade and earlier access to devices and reduce business compliance costs. In the short term, notwithstanding existing definitions, the TGA should give consideration to whether, for certain devices that are classified to a higher risk class in Australia than in Europe, some additional flexibility or abbreviated assessment/documentary evidence requirements may be appropriate. Any decision or ruling to facilitate more rapid approval would, however, need to be transparent and consistently applied across equivalent devices.

Problems associated with access to funding and reimbursement

Several concerns were raised about Government funding and reimbursement for medical devices. An overarching concern related to the fragmentation and overlap in these processes, including the need for streamlining the whole process of registration through to reimbursement (discussed separately below). Other concerns included:

- assessment of new medical procedures involving medical devices by the Medical Services Advisory Committee (MSAC) ‘continues to lack transparency and a sense of urgency’ (MTAA, sub. 23, p. 3) ‘in Medtronic’s experience it is not uncommon for a review to take over 2 years’ (sub. DR62, p. 3).

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- the requirement to re-submit a completely new application in the event that the Minister endorses a negative MSAC recommendation:

It would be more efficient if there was a re-submission process setup that did not require a new application and the subsequent time frame associated but rather an application process linking to the review conducted by MSAC previously. This will negate the requirement to commence an application and review from the beginning and minimise the duplication in the process. (Medtronic, sub. DR62, p. 3)

- the Prostheses List has not kept pace with innovation and this is distorting treatment decisions – there are some technologies on the List that many would not consider to be prostheses, and many other technologies that should be considered for reimbursement that are not reimbursed because they are not ‘prostheses’. ‘As a result treatment decisions are being driven by whether or not a particular therapy is reimbursed, rather than by a decision based on the most appropriate procedure’ (MTAA, sub. 23, p. 4). Johnson and Johnson Family of Companies had a particular concern that there ‘is currently no reimbursement mechanism that permits high cost, single use devices to be covered by health funds’ (sub. DR70, p. 21).
- inconsistencies in access to funding arrangements for a range of ‘essential care’ items – some items receive reimbursement or subsidy from the Australian Government, some from state governments and some none at all.²⁵
- inequity in access between privately insured and uninsured (public) patients to preferred technologies:

The current operation of the Prostheses List is widening that inequity by creating increasing numbers of gapped items for insured patients who may need to access a preferred technology recommended by their clinician. (Medtronic, DR62, p. 2)

Assessment

Regarding the MSAC processes, the Commission notes that current concerns are not new. Submissions to an internal review of MSAC conducted by DOHA in 2004-5 identified five major areas for improvement:

- clear reasons for decisions
- consistent use of evidence
- timely decisions
- including others in the process
- information and communication.

²⁵ Essential care items are those necessary for the care, well-being or, in some cases, survival, of patients.

The MSAC identified and agreed to 37 action items relating to these areas (DOHA 2006) and a number of reforms have been implemented that have gone some way toward addressing concerns, but overall MTAA are of the view that ‘[i]mprovements that might have resulted from MSAC’s review of itself have not eventuated’ (sub. 23, p. 3).

The MSAC should commit to clear timeframes for its assessments and identify further measures to improve efficiency and enhance transparency of its processes. MSAC processes would, however, benefit from independent external review.

The Doyle Review of Prostheses Listing Arrangements reported to the Minister in October 2007 and made recommendations that would result in a streamlined listing process (discussed below) and reduced administrative burden and red tape (Doyle 2007). The Report was generally supported by industry, but there has been no formal Government response and ‘reimbursement processes have not improved’ (MTAA, sub. 23, p. 3). DOHA advised that it is implementing a process of continuous improvement for the prostheses arrangements.

Expert clinicians are completing grouping work – sorting similar prostheses into groups to inform benefit negotiations. The outcome will be a comprehensive framework that ensures similar benefits for products with the same clinical outcomes, and a less burdensome application and assessment process for manufacturers. (pers. comm., 12 June 2008)

MTAA (sub. 23) proposed the establishment of an ‘Essential Care List’ that would operate in a similar manner to the PBS scheme for pharmaceuticals for a range of products that come within acceptable parameters of essential care. Johnson and Johnson Family of Companies also supported this type of list and claimed this ‘would allow for consistency in a reimbursement process that is defined by a set of criteria based on improved health outcomes, and not by whether a device is a ‘prosthesis’...’ (sub. DR70, p. 21).

The Commission recognises a need to achieve greater consistency and transparency in funding/reimbursement arrangements across Australia. However, there are a number of competing policy objectives in this area, including ensuring clinical effectiveness and promoting cost effective use of technologies. The Commission sees a particular need for a more holistic view to be taken when making assessments of devices/health technologies, including the need to take into account a broad range of societal costs and benefits – for example, longer term health benefits and reductions in costs to the health system overall. However, the design of an appropriate scheme requires detailed consideration and extensive consultation and is beyond the scope of this review.

Consideration of the Essential Care List proposal, prostheses listing arrangements and the operation of MSAC require further independent review. This would be best undertaken in the context of a broader review of Health Technology Assessment processes for devices (see below).

Multiple and overlapping processes

Participants raised concerns about the overall complexity of the Health Technology Assessment (HTA)²⁶ System in Australia. The complexity is apparent from figure 1. Even this somewhat simplified diagram gives a clear indication of the number of bodies involved and the difficulty interpreting their respective roles and responsibilities.

Johnson and Johnson Family of Companies submitted:

Whereas other countries with larger healthcare sectors have only one HTA body, Australia has four (five, if the Pharmaceutical Benefits Advisory Committee is included) government funded HTA groups. With the overlapping objectives of the TGA, MSAC, PDC and ASERNIP-S, and their responsibilities unclear, it is essential that regulations relating to funding and reimbursement decisions are streamlined to reduce inefficiencies and excessive delays in access to new technology avoided due to duplicated assessment processes. (sub. DR70, p. 20)

Similarly, Medtronic saw a need for a streamlined, transparent and accountable process for the registration, assessment and reimbursement of new medical technologies and advocated ‘the parallel review of medical devices for regulatory approval by the TGA, review by MSAC for the service associated with a medical device and review of the medical device for listing on to the Prostheses List’ (sub. DR62, p. 4).

The MTAA (sub. 23) continues to have concerns about the overall Health Technology Assessment (HTA) and the fragmented and duplicative nature of aspects of the current processes for registration and assessment for funding and reimbursement. Specific concerns raised with this review, include:

- products must undergo multiple assessments for regulatory and reimbursement purposes ‘There continues to be a lengthy, sequential pathway to bring medical technology to the patient through mandatory regulatory requirements, procedural review by MSAC, and reimbursement examination for the Prostheses List’ (sub. 23. p. 3)

²⁶ Health Technology Assessment (HTA) refers to the process and mechanisms designed to ensure safety, efficacy, effectiveness and cost effectiveness in health service delivery (PC 2005b, p. 178).

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- it is necessary to provide similar conformity clinical trial and investigation information to different government agencies due to a lack of coordination and understanding
 - processes take insufficient account of differences in complexities of medical technologies.

Assessment

These concerns have been raised with other reviews, including the Commission's Review of the Impacts of Advances in Medical Technology (PC 2005b) and the Regulation Taskforce.

The Commission's 2005 study found that health technology assessment processes were highly fragmented, leading to inefficient duplication and unnecessary costs and delays and that procedural transparency needed to be improved. The Commission also found that many of the states and territories have instigated their own bodies to advise on the use of medical technologies in hospital settings and the roles of these bodies (for example, the Victorian Policy Advisory Committee on Technology) partially overlap with various bodies at the Australian Government level, including MSAC and its advisory bodies and also duplicate assessments conducted by the PDC.

The Regulation Taskforce also recognised the need to improve regulatory arrangements for medical devices and endorsed a recommendation in the earlier Commission study for a major review of Health Technology Assessment. The Taskforce (2006) recommended that:

The Australian Government should undertake a system-wide, independent and public review of health technology assessment, with the objective of reducing fragmentation, duplication and unnecessary complexity, which can delay the introduction of beneficial new medical technologies. Health technology assessment processes and decisions should also be made more transparent, in line with good regulatory practice. (recommendation 4.22)

The Government accepted the Taskforce's recommendation (Australian Government 2006, p. 11), but the review has not commenced.

The Medical Devices Industry Action Agenda (DITR 2006) also highlighted the need for more coordinated and systematic health technology assessment, including the need for better synchronisation between the TGA and the PDC (box 4.2).

More recently, the Doyle Review of Prostheses Listing (Doyle 2007) recommended streamlining processes by allowing concurrent applications for TGA registration and inclusion on the Prostheses List. The review noted that the Prostheses and

Devices Committee should not require evidence of the safety and performance of devices as assessment of this information is the responsibility of the TGA.

MSAC also assesses procedures and technologies in relation to safety and effectiveness, potentially overlapping with prior assessments of safety and performance by the TGA.

Box 4.2 Impact of inefficiencies in HTA on timely access to devices

The Medical Devices Industry Action Agenda stated:

The assessment and negotiation processes managed by the Prostheses and Devices Committee generally take four and a half months from the time applications for listing close to when the new List is released. However, if listing on the ARTG occurs after a cut-off date for an application cycle, then listing on the Prostheses List can take up to eleven months. Product reimbursement is limited during this time as consumers and hospitals will be reluctant to purchase a device if it is not reimbursed by private health insurance. If approval by the Medical Services Advisory Committee is also required, that approval process can take up to 21 months in exceptional circumstances, although these times are expected to decrease as the recommendations of the recent review of this committee are implemented.

The best-case timeframe for a product to reach market is 18 months, if it is required to pass through the TGA, Medical Services Advisory Committee and Prostheses and Devices Committee processes in sequence; the worst-case timeframe is 40 months.

Source: DITR (2006, pp. 26-27).

Within the existing framework there is significant scope to streamline application processes across the different HTA bodies. Currently businesses are required to supply the same information in different formats to separate agencies. Consideration needs to be given to standardising information requests and, if possible, allowing businesses to submit the information once, to the TGA, which would then make the information available for use by MSAC, the PDC or other bodies.

Some general framework reforms were being drafted as part of the development of the proposed joint Australia New Zealand Therapeutic Products Authority. With the indefinite suspension of negotiations on the establishment of ANZTPA, the Commission understands that the Government has been considering the most appropriate process for addressing concerns about the regulatory and reimbursement systems. DOHA provided the following information on recent developments:

The Department is putting advice to the Minister for Health and Ageing on options for a review of Health Technology Assessment in the broader context of strategic health reform, incorporating ideas from the 2020 Summit and the National Health and Hospital Reform Commission's agenda.

At the same time, work to reform HTA processes outside of a public review framework has continued. The objective of the reforms is to improve the timeliness of patient

access to beneficial technologies without comprising patient safety or value for money. These reforms are consistent with the medical device industry's urging for shortened assessment timeframes and reduction in 'red tape', through the introduction of better risk management and information sharing strategies. (pers. comm., 5 June 2008)

RESPONSE 4. 8

The Australian Government should commission a comprehensive and independent public review of the overall Health Technology Assessment (HTA) System for medical devices/technologies as soon as possible. The review should examine regulatory and policy frameworks and processes impacting on access to, and use of, devices and technologies.

Outcomes should include options to improve the efficiency, transparency and timeliness of processes for assessing safety and performance, and suitability for public funding and reimbursement by private health funds, including:

- *streamlining the overall HTA framework to remove duplication and overlap*
- *addressing inconsistencies in prostheses listing arrangements, which can impede the introduction of new technologies and distort treatment decisions*
- *improving the operations of the Medical Services Advisory Committee.*