MEDICINES Australia

BETTER HEALTH THROUGH RESEARCH AND INNOVATION

31July 2008

Commissioner Michael Woods
Regulatory Burdens Review
Productivity Commission
GPO Box 1428
Canberra City ACT 2601

By email: regulatoryburdens@pc.gov.au

Dear Commissioner

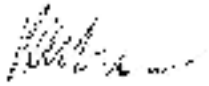
Thank you for the opportunity to reply the Productivity Commission's Draft Research Report on the Annual Review of Regulatory Burdens on Business – Manufacturing and Distributive Trades. Please find attached Medicines Australia's follow up submission in response to the Draft Report.

In this follow up submission responding to the Draft Report, Medicines Australia would like to respond to issues of regulatory burden which were raised in our initial submission and considered in the Draft Research Report with a view to elaborating and clarifying identified issues. These issues include:

- Good manufacturing practices;
- TGA and PBAC registration and listing process
- Proposal for PBS cost recovery
- Weighted Average Monthly Treatment Cost (WAMTC) measures
- Medicines Australia's Code of Conduct;
- Intellectual property framework;
- Harmonisation of multi-centre ethics approval ; and
- Correction to Figure 4.1

I trust that these comments are of assistance in your consideration of this matter. I would be happy to discuss these matters further with you at your convenience. If you have any queries on the submission, please contact Michael Fitzsimons, Policy Manager, at Medicines Australia on 02 6122 8500 or at michael.fitzsimons@medicinesaustralia.com.au.

Yours sincerely



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Medicines Australia's Submission to the Productivity Commission

Response to the Draft Research Report: Annual Review of Regulatory Burdens on Business – Manufacturing and Distributive Trades

Medicines Australia would like to address some issues arising from the Draft Research Report released by the Productivity Commission. Medicines Australia identified a number of areas where clarification or further input may be useful to the Commission and have addressed them in this response.

The pharmaceutical industry bears a significant regulatory burden. In order for a medicine to become broadly available to the public, a long and onerous process must be undertaken through regulatory channels, as illustrated in the Draft Report in Figure 4.1. This burden is arguably higher than the one faced by most other manufacturing industries. It applies at all steps of the product life cycle, during the R&D phase, prior to bringing a medicine to market, during the evaluation processes for registration and reimbursement, and then subsequent ongoing post market monitoring while the product is on the market. Even the process of removing a product from the market involves a significant level of regulatory control. Medicines Australia understands the need for careful and complete evaluations to be performed on pharmaceutical products to ensure that the public can rely on their quality, safety and efficacy. Nevertheless, Medicines Australia also believes that the pharmaceutical industry is subject to regulatory burden significantly in excess of other areas of the health care system and other manufacturing industries. Efforts to achieve efficient and timely processes should be paramount in policy consideration.

Most medicines are significantly subsidised for the Australian public by the Federal Government. The Pharmaceutical Benefits Scheme (PBS) is a public health insurance program designed to provide equitable access to medicines for all Australians. In order to determine which medicines are listed on the formulary, they must undergo a complex evaluation process. Medicines Australia agrees with comments raised by Pfizer in Box 4.4 of the Draft Report. The Pharmaceutical Benefits Advisory Committee (PBAC) undergoes increasingly complex evaluations and this adds to the regulatory burden companies face in preparing submissions for evaluation.

Therapeutic Goods Regulation

Medicines Australia notes the Commission's observation that the Therapeutic Goods Administration (TGA) is undertaking an internal review of its business processes.

Medicines Australia would like to re-iterate the importance of action and reform following such a review. The TGA's initial examination of business

processes was commenced in 2002 and the M P Consulting Workflow Practices Report on the Drug Safety and Evaluation Branch (Now: Office of Prescription Medicines) was completed in 2006. Yet to date there has been little progress in implementing the recommended reforms.

Medicines Australia acknowledges that the breakdown of the joint Australia New Zealand Therapeutic Products Agency (ANZTPA) negotiations may have impacted on this, as have the changeover of TGA National Manager and the change of Federal Government.

Medicines Australia further re-iterates the requirement for increased transparency in the TGA processes of both; medicine evaluation and; auditing of manufacturing facilities.

Medicines Australia additionally notes the Regulatory Reform Consultations being conducted by the TGA during July and August 2008, to which members of industry have been invited. These consultations point to a renewed commitment on the part of the TGA to implement the workflow practices reforms and this is very welcome. The priority is now to ensure that the reforms are finalised and implemented in a timely manner and in partnership with the industry.

Occasionally, reforms to processes require the one off investment of additional resources to implement those reforms. Should the implementation of TGA workflow reforms require an investment into TGA resources, Medicines Australia recommends that the TGA be permitted to run down its current surplus funds to achieve this end without requiring additional fee or levy increases to cover the cost of these reforms, thereby adding additional regulatory cost to the industry.

With regard to the TGA conduct of desktop audits of overseas manufacturing sites, Medicines Australia acknowledges and welcomes the TGA Office of Manufacturing Quality's (OMQ) agreement to publish their 'general risk-matrix' to provide greater clarity to industry on the rationale for auditing decisions.

Medicines Australia acknowledges the OMQ's current problem of lack of personnel resources and accepts that OMQ is actively recruiting to address these short-falls. Medicines Australia further acknowledges OMQ's commitment to improving, and widening, its international recognition arrangements and the 'Smart GMP Regulation initiative'. Medicines Australia is keen to work in partnership with the OMQ to solve the current backlog of approval processes.

Medicines Australia recommends the OMQ work towards greater transparency in order to provide some predictability in the scheduling of audits, and in the timelines for completion of auditing activities; particularly desk-top audits of overseas manufacturers. The preferred goal would be the institution of predictable timelines (mandatory and/or achievable), once OMQ's personnel and resourcing restrictions have been resolved.

Medicines Australia would like to request that a comprehensive document be produced by OMQ identifying '*common deficiencies'* in applications for desk-top audits. The number of incomplete or deficient applications, received by OMQ, and subsequent negotiations between OMQ and applicants to resolve the deficiencies, was suggested by the TGA to be a significant contributor to the backlog of incomplete audits. A document highlighting common deficiencies would assist companies in their preparation of applications and would likely reduce the number of deficient applications made. It is logical to extrapolate that a reduction in deficient applications would consequently reduce the regulatory and time burden to both parties. Medicines Australia would welcome the opportunity to work with the OMQ in developing this document.

TGA Registration and PBS Listing Processes

Medicines in Australia are required to have a positive recommendation in the TGA Delegate's summary and request for ADEC advice before they are able to seek listing through the Pharmaceutical Benefits Advisory Committee (PBAC) for subsidy on the Pharmaceutical Benefits Scheme (PBS).

The Commission's Draft Report suggests consideration is given to a system whereby PBAC evaluation of medicines can commence earlier in the TGA evaluation process before a final TGA recommendation on registration is available. The Commission has suggested that companies could pay for a parallel regulatory and listing process. The report infers that companies could pay extra for an earlier consideration of their medicines for reimbursement on the PBS. The suggested rationale for this is to prevent or minimise the risk of a medicine not gaining ARTG approval subsequent to significant Government resources being utilised for PBAC evaluation.

Medicines Australia argues that imposing a charge for parallel evaluation effectively replaces one regulatory burden (slowing the access of medicines due to a lengthy listing process) with a new one (a form of insurance charge). This outcome is not desirable. Nor is it clear that having the option to start the PBAC process earlier before TGA approval would impose any additional costs on Government. Medicines Australia does not believe that there would be a significant additional cost to Government if parallel TGA and PBAC evaluation were provided as an option for companies to utilise. Medicines Australia understands 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.

The Commission suggests that PBS cost recovery measures would provide an incentive for companies to not seek PBAC review if they had a measure of risk in not obtaining ARTG approval (PC Draft Research Report p. 78).

This measure is unnecessary. Companies already face significant costs when preparing a PBAC submission – somewhere between $150K and $500K, depending on the complexity of the submission. These administration

costs already act as disincentives to the pursuit of unlikely PBS listings; that is, the existing significant cost of preparing a submission already acts as a financial barrier to companies putting forward applications for PBS reimbursement that risk not achieving ARTG listing.

Proposal for PBS Cost Recovery

Since the preparation of Medicines Australia's first submission to the Commission's inquiry, the Federal Government announced in the 2008 Federal Budget its intention to introduce a full cost recovery process for the PBS evaluation process. [1,2] This process, if implemented, would introduce a substantial additional regulatory cost on Australia's pharmaceutical industry and, in all likelihood, lead to some medicines not being listed on the PBS. Medicines Australia opposes the introduction of cost recovery arrangements for the PBS evaluation process because they[3]:

1. have the potential to restrict access to medicines for some Australians, most importantly children, cancer sufferers, the dying and Aboriginal and Torres Strait Islanders, thus contradicting Australia's National Medicines Policy;
2. are not accompanied by any proposals and/or performance targets to ensure improvement in the efficiency or timeliness of the PBS listing process;
3. are likely to deter innovation in the Australian pharmaceutical industry by creating additional barriers to investment in an industry that, as recent Productivity Commission reports have shown, is already one of the most heavily regulated in Australia; and
4. do not conform to the standards and requirements contained in the Australian Government's Guidelines on cost-recovery arrangements.

Weighted Average Monthly Treatment Cost (WAMTC) measures

Medicines Australia recognises the Productivity Commission's concerns that taxpayer continue to get the best value for PBS listed medicines. Medicines Australia appreciates the Commission's recognition that current WAMTC arrangements imposed by the Government are burdensome. However, we

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[1] Proposed PBAC cost recovery measures (actual fees to be determined in the regulations):
- $120,000 for a major submission
- $13,000 for a minor submission
- $1,000 for a Secretariat Listing

[2] Proposed PBPA cost recovery for price negotiations:
- $6,000 for Tier 1
- $25,000 for Tier 2/3
- $500 for generic listing

[3] Medicines Australia submission to the Australian Senate Community Affairs Committee Inquiry into the *National Health Amendment* (Pharmaceutical and Other Benefits – Cost Recovery) Bill 2008, available at: http://www.aph.gov.au/Senate/committee/clac_ctte/nat_hth_pharm_cost_recover_08/submissions/sublist.htm

would encourage the Commission to reconsider the need for WAMTC policy in light of PBS reforms.

Recent reforms, which split the PBS formulary into two components – essentially one for patented medicines and one for the off-patent generic market, are designed to ensure taxpayers achieve the best value for medicines. Measures such as statutory price cuts and price disclosure, the latter itself containing administratively burdensome requirements, were introduced in order to lower the price Government pays for off-patent generic medicines.

Medicines Australia believes that continuing with the WAMTC process on top of these reforms will be an unnecessary measure in light of the reforms. 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.

Intellectual Property Framework

While Australia's intellectual property framework is generally respected, a range of issues add to the regulatory burden and cost for the pharmaceutical industry. A lack of sufficient data exclusivity, changes to section 26 of the Therapeutic Goods Act in 2006, and more importantly, a lack of proper enforcement of exclusivity provisions, has increased patent litigation costs for the originator pharmaceutical industry. Companies are increasingly forced to defend more valid patents against infringements than in the past, which adds to the cost of business.

The Commission argues that intellectual property issues are best considered by the Review of the National Innovation System (Draft Report, p. 85), and implies that these issues do not constitute a regulatory burden. However, an increase in unnecessary litigation, which can be largely avoided with proper enforcement, increases red tape and cost of doing business in Australia. Moreover, due to a lack of sufficient notification to innovator companies of s26b certificate filings, where originator companies are notified 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. The complexity and lack of enforcement in the system, particularly in the lack of notification to innovator companies of s26 certificate filings under the Therapeutic Goods Act, leads to a greater than necessary regulatory cost for industry.

Harmonisation of Multi-Centre Ethics Approval

The Commission also offers its assessment on the process of harmonisation of multi-centre ethical reviews of clinical trials in Australia (Draft Report, pp. 60-61). The Commission endorses the National Health and Medical Research Council's (NHMRC) work so far, and encourages the Council to continue its work.

Medicines Australia agrees that this work is important and would welcome the conclusion of the NHMRC work on harmonising such reviews. However, the key point is that this process has been ongoing for at least three years. No tangible progress on a nationally streamlined system has been made at this time.

Implementation of a national, streamlined ethical approval process for multi-centre trials is a major, positive change that can readily be achieved to support the continuing, very significant level of global clinical trial activity in Australia. This initiative has significant support amongst State Governments. With a commitment to complete the harmonisation work – especially from the NHMRC – it is readily achievable.

Medicines Australia offers its continuing support to the NHMRC to implement a national system of ethics reviews. However, there is a real need to urgently push forward with a national streamlined approach to multi-centre clinical trial approval as soon as possible.[4] 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.[5,6]

In view of the increasing commercial attractiveness, quality and capacity from emerging markets as a location for clinical trials, it is critical that Australia improve its global competitiveness. Improving the timeliness of approval to start a multi-centre trial in Australia is one clear opportunity that has been identified for at least the past three years.

Medicines Australia and the Pharmaceuticals Industry Council's (PIC) R&D Taskforce have been working with various States (most notably NSW, Victoria

[4] In one example, AstraZeneca Australia selected four sights to conduct a Phase IV [cardiovascular] clinical trial in December 2007. The company lodged applications for ethical approval of the trial at each of the four sites in January and March 2008. As of July 30, only two sites have been given approval by associated ethics committees. The company is awaiting responses from two other sites, which received applications for approval in March. AstraZeneca Australia has been unable to initiate this multi-centre clinical trial, and its parent company has recommended that it no longer pursue this trial in at least one of the sites..

[5] Australian Health Ministers' Advisory Council (AHMAC), September 2006, *A streamlined national approach to scientific and ethics review of multi-centre health and medical research in Australia, issues and options.*

[6] Pittman, K, July 2007, *Streamlining scientific and ethics review of multi-centre health and medical research in Australia*, report to the NHMRC.

and Queensland) on a range of initiatives to improve the timeliness for study start up by streamlining ethical process for multi-centre clinical trials within each State. NSW has been the first State to introduce a streamlined, multi-centre ethical approval process (in mid 2007). The experience with streamlined ethical approval in NSW to date suggests that ethical approval times had been improved, as anticipated, and these findings were supported by initial data from NSW Health Ethics as well as Merck Sharp & Dohme in their trials.[7]

The concern is that in the absence of a nationally harmonised system, the various State governments are currently going ahead and introducing their own State-based streamlined systems. Whilst we commend the States for implementing initiatives which will improve timeliness of obtaining clinical trial approval within a State, this should not be regarded as a viable alternative to a nationally harmonised system. Implementation of State-based systems risks undermining the impetus for pushing towards a nationally-based harmonised system.

There has been little real progress in the national approach beyond the release of the Pittman report on harmonisation in mid 2007,[8] and no progress has effectively occurred since then.

As recently as 19 May 2008, the NHMRC indicated to stakeholders including industry that they: a) would not be implementing all the elements of the Pittman report; b) did not yet have a clear implementation plan; and c) still had no clear timetable.

The industry is greatly concerned with the lack of progress towards a national system. Given the progress of State governments in implementing their reforms, there is a risk that the imperative of developing a nationally harmonised system will be lost.

Medicines Australia's Code of Conduct

Medicines Australia's self-regulatory Code of Conduct is authorised by the Australian Competition and Consumer Commission (ACCC). The Condition of authorisation requires member companies to report to Medicines Australia every educational meeting and symposia held or sponsored by each company every six months.

Medicines Australia welcomes the Commission's recommendations that the ACCC work with Medicines Australia to minimise the compliance burden arising from educational event reporting requirements (PC Draft Report p. 80).

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[7] Please note the final report of the 3rd R&D Taskforce Forum, held in April 2008. The report is available at www.pharmacouncil.com.au. Please especially note the Global Competitiveness Survey.

[8] Pittman, K, July 2007, *Streamlining scientific and ethics review of multi-centre health and medical research in Australia*, report to the NHMRC.

All Medicines Australia member companies are required to adhere to the Code or face sanctions for non-compliance. Currently only those sections of the Code that deal with advertising and promotion apply to all sponsors of prescription medicines, regardless of whether they are members of Medicines Australia. This is imposed by the TGA marketing approval letter.

However, other sections of the Code that deal with matters other than advertising and promotion, such as the supply of samples (starter packs), for example, or the provision of benefits such as hospitality and travel, do not apply to companies that are not members of Medicines Australia. Requirements imposed under the Code that do not apply consistently to all pharmaceutical companies place an excess compliance burden on Medicines Australia members over and above other suppliers of prescription medicines. It creates an uneven playing field that disadvantages Medicines Australia members for recognising and complying with changing community standards articulated in the Code.

In a recent submission to the National Health and Hospitals Reform Commission Medicines Australia recommended that, in order to maintain confidence in the ethical conduct of the entirety of the pharmaceutical sector, all companies marketing prescription medicines should be required to comply with the entirety of the Medicines Australia Code of Conduct as a condition of product licence (marketing approval).

Correction to Figure 4.1

Medicines Australia would like to draw attention to an error in Figure 4.1 on page 56 of the Draft Report. In the diagram, the box marked “PBA”, below the box marked “PBAC”, should read “PBPA” to reflect the common anagram of the Pharmaceutical Benefits Pricing Authority.