Submission to the Expert Review of Medicines and Medical Devices Regulation

January 2015
Contents

EXECUTIVE SUMMARY ........................................................................................................................ - 3 -
Review of the Current Status of Medicines Regulation in Australia................................................... - 5 -
Creating a ‘Fit-for-Purpose’ Regulatory System in Australia ............................................................... - 5 -
Opportunities for Harnessing Efficiency ............................................................................................. - 6 -
i. Optimising Work Sharing Activities with Overseas Regulators............................................... - 6 -
ii. Creating multiple approval pathways ..................................................................................... - 8 -
iii. Delivering on New Information Technology Capabilities ..................................................... - 10 -
iv. Eliminating Unnecessary Red-Tape and Duplication ............................................................ - 12 -
   i. Pre-Submission Planning Stage ......................................................................................... - 12 -
   ii. Management of Post-Approval Changes .......................................................................... - 12 -
   iii. Parallel Processing ............................................................................................................ - 13 -
   iv. Duplication in State and Territory Medicines Regulation ................................................. - 14 -
   v. Cost Recovery .................................................................................................................... - 14 -
   vi. Clinical Trials ..................................................................................................................... - 15 -
CONCLUSION ..................................................................................................................................... - 16 -
EXECUTIVE SUMMARY

Medicines Australia is the peak body representing the research-based pharmaceutical industry in Australia. Medicines Australia member companies are responsible for the discovery, research, development and commercialisation of up to 86% of registered prescription medicines available to Australian patients (via the Pharmaceutical Benefits Scheme, by value).

Medicines Australia looks forward to being a partner in the evolution of our current world class system, and welcomes the opportunity to provide information and perspective to this initial stage consultation and development phase.

The purpose of this submission is to assist the Review Panel to identify ways to restructure Australia’s regulatory framework so that it is fit-for-purpose and globally competitive. The review provides a timely opportunity to enact meaningful reforms by reconsidering Australia’s approach to medicines regulation, thereby harnessing significant efficiency gains, reducing unnecessary red tape and delivering real savings to the benefit of government, patients and industry.

Medicines Australia recommends:

1. **Optimising work sharing activities with overseas regulatory agencies** to increase efficiency. This includes the ability to adopt international decisions from trusted regulators where appropriate; and ensuring Australia upholds public health and safety through sovereign decision making.

2. **Creating multiple approval pathways** including fast-tracked, priority registrations, breakthrough medicines and re-establishing flexibility.

3. **Delivering on long-promised information technology capabilities** including eCTD, communication portals between the TGA and sponsors, and a robust system of application tracking to ensure optimal operational efficiencies for both government and industry; and

4. **Eliminating unnecessary red tape in the registration system** related to unnecessary data requirements for pre-submission and unwarranted duplication in Australian specific requirements in Module 1, and duplication in state and territory poisons legislation.

Because there has been limited time to consult with the industry and respond to such a complex review, Medicines Australia is willing to provide additional information to the Review Panel if required, to clarify any of the recommendations made.

Medicines Australia acknowledges full support for the five stated principles underpinning the Review. The principal role of regulation is to **protect public health and safety**. Therefore, an approach based on the risk posed by each therapeutic product is appropriate. This should encompass the whole of the lifecycle of a product with an emphasis on post-market monitoring.
Australia must retain its capacity to undertake independent assessments of therapeutic goods, with this responsibility remaining with the Commonwealth of Australia.

Any changes proposed to the current system must be firstly focussed on ensuring the internationally recognised standard for regulation in Australia is retained, albeit through a system driven by efficiency with the necessary resources to deliver continuous improvement to keep pace with medical developments.

The overall regulatory system for medicines access in Australia encompasses both the registration of medicines for market and the assessment of medicines for subsidy under the national health insurance scheme, the Pharmaceutical Benefits Scheme (PBS). As the existing Australian medicines registration system interacts closely with the Commonwealth reimbursement system, Medicines Australia will need to consider how any changes in registration practice affect the timely and equitable access to subsidised medicines and medical devices.

Furthermore, any changes aimed at improving regulatory processes and reducing regulatory burden (in line with the Government’s innovation and competitiveness agenda) should not result in unexpected or unnecessary delays in the availability of products for Australian patients. For example, delays caused by waiting for overseas regulatory decisions in cases where domestic regulatory practices would be more efficient and timely or achieve a better outcome for patients.

Therefore, this submission will:

- review the existing regulatory processes and highlight efficiencies that should be retained;
- create a refreshed and fit for purpose regulatory framework;
- identify efficiencies from partnering with other jurisdictions; and
- recommend improvements to the registration and monitoring of medicines to safeguard public health and safety for Australians; modernise the regulatory processes and eliminate unnecessary red tape and duplication.

Detailed recommendations are provided throughout the submission, indicated by grey boxes. A separate table of complete recommendations is provided in Attachment A and answers to the questions from the discussion paper are provided as Attachment B.
Review of the Current Status of Medicines Regulation in Australia

The Australian Therapeutic Goods Administration (TGA) is globally recognised as a sophisticated regulator. This is reflected in the existing international partnerships with other key agencies including the European Medicines Agency (EMA), the United States of America’s (US) Food and Drug Administration (FDA) and Health Canada. It is also regarded as a benchmark agency and role model in the Asia Pacific region. These partnerships are critical to ensuring a globally harmonised approach to regulation that facilitates timely access to new medicines for the Australian public. Enhancing harmonisation offers opportunities for further efficiencies.

Currently, the infrastructure of the TGA covers all aspects of medicines regulation and extends beyond evaluation and assessment of applications to register medicines. The TGA plays a critical role in the monitoring and compliance of medicines supplied in Australia, including good manufacturing practice (GMP) inspections both in Australia and overseas, and the post market safety monitoring and investigation of products, known as pharmacovigilance.

However, Australia lags behind comparable nations with advanced regulatory capability in many areas, and this review provides the opportunity to reassess and restructure.

Creating a ‘Fit-for-Purpose’ Regulatory System in Australia

Medicines Australia supports an Australian regulatory system that is fit-for-purpose; one that is adaptive and responsive to changes in business and technology, provides an appropriate level of public health protection and is efficient and cost-effective for both government and industry.

The forfeiture of flexibility in the process that occurred in 2010 to streamline processes has instead created a unique barrier to medicines entry in Australia. The inflexible process denies sponsors and patients opportunities for early access to breakthrough medicines. Current data indicates that medicines evaluations take just as long as they did prior to the introduction of the 'streamlined' process.

---


2 Extensive consultation with multiple stakeholders, including the wider pharmaceutical industry, occurred between 2004 and 2007 as part of the negotiations for a joint ‘Australia New Zealand Therapeutic Products Agency’ (ANZTPA). When these negotiations were indefinitely postponed in 2007, the Australian Government agreed to introduce reforms of the TGA processes, based on the consultation findings, in an ‘Australian-only context’.

This resulted in the implementation of the Business Process Reforms, including a 'streamlined' prescription medicine registration process in 2010. The structural reforms, introduced with industry support, delivered some degree of predictability of evaluation timelines, as intended.

It was assumed that the revised process, in which a well understood data set, evaluated within a more rigid framework with set milestones and timelines, would deliver faster approval times despite the loss of flexibility for both industry and the agency.
This brings into question the current constraints in decision making that can result in unwarranted delays to patients getting access to new treatments. As such, this review is a timely opportunity to restructure processes; ensure faster timeframes for medicines registration; and re-establish flexibility to meet growing need.

Continuous and rapid advancements in the development of medicines and technologies require Australia to have an adaptive and forward-thinking regulatory capability. In this regard, the regulatory system must be further restructured and continuously improved with the needs of the future in mind.

A fit-for-purpose system for the registration of medicines should be as transparent as possible to provide government, patients, health care providers and industry with confidence in the rigor and reliability of the regulators decisions.

The efficiency of the process must be demonstrated by transparent and robust reporting of metrics that include benchmarked access to medicines (the time it takes for them to become available to Australian patients through marketing approvals) compared to similar jurisdictions.

The processes for marketing approvals should be restructured to allow a variety of decision-making pathways, while still putting the public health and safety of Australians uppermost.

Opportunities for Harnessing Efficiency

There are numerous opportunities to improve efficiencies in the framework and processes for medicines and medical devices regulation in this country.

1. Optimising Work Sharing Activities with Overseas Regulators

Recommendation:

Implement a formal, transparent mechanism for work sharing with similar overseas regulators, including integration with and access to, international assessments.

Allow the adoption of decisions from trusted regulators with Australian sovereign sign-off, in circumstances where the overseas decision results in faster access to breakthrough treatments

Retain full assessment and decision-making capacity in addition to revising mechanisms that currently exist

Medicines Australia asserts that there is a need to retain the ability of the Commonwealth of Australia to make sovereign decisions on marketing authorisations, in the interests of public health and safety.

Medicines Australia also contends that Australia requires domestic capacity to complete local pre-marketing processes for medicines registration.

---

3 The regulatory framework model adopted by Norway and Iceland (see reference 5 below).
Medicines Australia recommends that the range of evaluation processes is extended to allow the adoption of international decisions made by trusted overseas regulators. Medicines Australia members have advised that a number of factors will determine the suitability of adopting an overseas decision including the availability of other approval pathways and the type of application and its applicability to the Australian local context.

However, Medicines Australia recommends that the option for the TGA to endorse applications based on FDA or EMEA approvals would be most beneficial for products that had undergone expedited review.

In 2013, 40% of new molecular entity applications were evaluated by the FDA through an expedited review process (11 of 29 applications), with a median 125 days faster approval time than standard FDA approvals. For the EMA, 10% of new molecular entity applications were evaluated through an expedited review process in 2013 (3 of 30 applications), with a median 145 days faster approval time than standard approvals by the EMA.

Not all of these medicines have subsequently sought registration in Australia. However, adoption of decisions such as these has significant potential to reduce duplication by Australian regulators; eliminate unique Australian requirements; reduce regulatory burden and costs, and facilitate expedited access to innovative medicines for Australian patients.

Medicines Australia has identified the following countries as currently operating with comparable regulatory standards for medicines, and from which decisions and work-sharing arrangements may offer reciprocal benefits for industry and government as trusted regulators:

- European Union (EU);
- United States of America (USA);
- United Kingdom (UK); and
- Canada.

Sharing capability and expertise rather than relying exclusively on other regulators for all applications means that government, patients and industry in each country can benefit from the arrangements.

---


5 The regulatory framework model adopted by Norway and Iceland, which are not members of the European Union (EU), demonstrates one useful example of a work-sharing approach. These countries are fully integrated into the EU’s centralised procedure for evaluating new medicines, thus benefitting from the scientific expertise and resources of the broader European community to support a parallel national decision on regulatory approval. The full dossier is provided to both regulatory agencies operating under a work sharing arrangement. This ensures that the local agencies maintain a state-of-the-art knowledge base and capability, without having an excessive work burden that could unnecessarily delay access to new medicines. Under such a model, Australia would act as an integrated ‘member state’ of the EU (c.f. Norway/Iceland). Australia would receive the full submission from the sponsor and the draft assessment report from the evaluator (c.f. member states). The Australian regulator would review the evaluation report to specifically assess the applicability to Australian clinical practice (there may be opportunity to refer to an advisory committee) and identify any other major concerns that might not support marketing authorisation in Australia. There would be opportunity for the sponsor to then respond to the evaluation report and the Australian regulatory assessment. The Australian regulator would then take the application through to completion of a marketing authorisation decision for the Australian market.
Proposals have been publicly discussed to replace the Australian pre-market evaluation process with the adoption of decisions made in other jurisdictions such as Europe or the US. There are notable cases where this would be a reliable approach. However, there are also cases where this would result in unnecessary delays in patients getting access in the Australian market, such as, if Australia had to wait until a final decision is made in another jurisdiction before access could be provided here.

The forfeiture of capacity for local assessments and decisions would also have an immediate and obvious consequence for companies not intending to make an application in selected overseas jurisdictions, or not in the first instance (for example, Australian biopharmaceutical companies and other small companies that lack a significant presence outside the Asia Pacific region).

As such the adoption of international decisions should be seen as a supplement to Australia’s regulatory processes and not as a replacement.

It will also be necessary to establish an agreed process to identify trusted regulators and to assist in country selection when Australia seeks to adopt an international decision, as decisions frequently differ across countries and vary according to accepted clinical practice within those countries. This will require added consultation and scrutiny of likely consequences to the Australian public.

ii. Creating multiple approval pathways

Recommendation:

Restructure and modernise the registration pathways to incorporate flexibility, commensurate with the risk, benefit and assessment needs.

Implement multiple registration pathways and redesign categorisations to enable fast track options, breakthrough designations, rolling data provision and streamlined processes for less complex submission types (this would require appropriate work streams and stakeholder consultation to ensure efficiencies are identified and captured)

Re-establish flexibility within the revised registration pathways

Emphasise post-market and pharmacovigilance activities to ensure the Australian community has confidence in the quality, safety and efficacy of therapeutic products in Australia

Multiple approval pathways are necessary within Australia to enable the adoption of international decisions, to modernise local regulatory processes and reduce regulatory workload, duplication of effort and speed up access.

---

6 For example, as stated, where there has been an accelerated review overseas, or where there are added indications for an Australian registered product with sufficient post-market experience to assure safety and efficacy in Australian patients.

7 An example of differences in clinical practice is the availability of therapies for first line use in treating Multiple Sclerosis in Australia that are only available for second line use in the USA.
Adoption of decision from overseas trusted regulator: Automatic adoption of a trusted international decision (as detailed in the previous section) should be at the request of the sponsor and should follow an expedited process with specific acceptance criteria. This model would be appropriate where the sponsor and the Australian regulator are satisfied that the international decision has adequately accounted for all potential benefits and risks that are relevant to the Australian population, so that public health and safety would not be compromised. The sovereign decision to accept the approval would remain with the Commonwealth of Australia through the TGA.

Conditional approvals: Granting of conditional approvals for medicines could occur based on limited data, where the data available at the time of application does not include the complete development programme or before the phase III clinical programme has been completed and analysed. The terms for providing and evaluating the emerging data would be included in the conditions for registration\(^8\).

Breakthrough designation: Accelerated evaluation timeframes for breakthrough therapeutic advances or to support technologies such as health applications or diagnostics that enhance quality use of medicines and minimise risks, could be modelled on the EU Accelerated Assessment or US Priority Review mechanisms.

In 2013, the difference in median approval time between expedited and standard review was 320 days for Swissmedic; a difference of 145 days was observed for EMA and Health Canada, and approximately 125 days for PMDA and FDA\(^9\).

Rolling data: Flexibility should be re-established in the registration process to facilitate early applications and shorter review timelines. This refers to a process formerly known as ‘rolling submissions’, where the initial submission is made with available data and, as more mature data becomes available it is submitted, accepted and evaluated by the TGA during the ‘rolling’, ongoing evaluation period. The full data-set is evaluated prior to the final decision. This may significantly accelerate access to new products in Australia.

Parallel work sharing: Expanded work sharing should be established that enables parallel submission with overseas regulators, with the retention of local decision-making authority by the TGA. Under such a proposal, two or more partner regulators (such as FDA, EMA and TGA) would share the evaluation of a single submission such that the assessments are conducted by one regulator on behalf of the others and the assessment is shared across all regulators in the arrangement. The approval decision would still be made by the TGA but can be granted at the same time as the other regulators. This would enable Australian patients to have access to medicines at the same time as patients in the US or the EU.

---

\(^8\) Eligibility criteria for advanced registration pathways such as these could be aligned with those being applied in the accelerated pathways of the US and EU. This would assist the TGA to assess requests, and facilitate submission of the same dataset across jurisdictions. This would further ensure the consequent relevance of US/EU evaluation reports if required to assist in decision making and would reinforce work-sharing options.

Medicines Australia also contends that there are a number of other submissions that could be processed more efficiently, freeing up resources to focus on the more complex submissions or varied submission pathways in the system.

*Generic applications:* Submissions for generic medicines and variations to existing products are currently evaluated through the existing Category 1 process which is the same as for new chemical entities and results in lengthy delays in deciding on significantly less complex datasets.

*Down-scheduling:* There are also potentially unrecognised opportunities to down-schedule prescription medicines to either pharmacist-only or self-selected over-the-counter access. A reliable process pathway to identify and enable such decisions to be made efficiently and in a timely way would deliver real savings to industry and government and better access for patients.

The aim of the Australian regulator must be to enable rapid access to safe and effective medicines, particularly those that will address unmet medical needs of patients and are in the interest of public health. Australia must ensure it meets community expectations in this regard.

The transparency of these types of processes and approvals should be sufficient to support the role of patients and prescribers in informed decision making when seeking to access these therapies.

Under a restructured regulatory system there would be a redesign of the categorisation system to enable clear differentiation between different pathways for evaluation, including an understanding of the resources required for each pathway.

Medicines Australia recommends flexibility for sponsors to select the most appropriate process for the particular registration applications.

Enhanced post-marketing and pharmacovigilance activities will need to be reviewed and redesigned to meet the needs of an adaptive, flexible and advanced regulatory process. This will be particularly relevant on the introduction of rapid and early access pathways and should be designed to meet the Australian community’s expectations for transparency and reliability of information.

Entering into more meaningful work-sharing arrangements with overseas agencies that have legal and regulatory means for assigning breakthrough status, fast-tracking review, and/or use adaptive approaches to licensing will facilitate faster access to breakthrough medicines in Australia.

### iii. Delivering on New Information Technology Capabilities

**Recommendation:**

*Implement high performance and up-to-date IT infrastructure to support the Australian regulatory system, enhancing communication as well as supporting the efficient and transparent management of registration applications and providing appropriate levels of transparency to the community.*
Australia lags behind comparable nations in this area. For example, despite years of promises, and unlike all the major medicines regulators, Australia still has no efficient electronic lodgement and evaluation system (e-CTD). This means that Australian sponsors are required to produce and submit paper-based submissions just for this country. This is a significant barrier to efficiency and an unnecessary cost and regulatory burden.

Implementing full e-submission capability is critical to realising efficiencies in work flow, increasing transparency and optimising resource utilisation for both the agency and industry. However, the existing TGA infrastructure does not currently support transition to an e-submission working environment in an expedited manner.

The adoption of appropriate technology solutions to support eCTD will enhance efficiency and resource utilisation for both industry and the agency. To do this successfully, emerging e-solutions internationally need to be assessed and a plan developed to ensure that Australia keeps pace with comparable international jurisdictions upon whose relationships the restructured system will rely.

The current lack of effective IT infrastructure is a significant barrier to efficient working practices and contributes to delays in information transfer between sponsors. An additional administrative burden is created by the lack of an electronic work flow that provides sponsors with ‘real time’ information on the progress of applications.

IT capability has the capacity to eliminate burdensome manual processes, delivering time and cost savings to government and industry. A robust system of application tracking would record the entire product lifecycle history and automatically provides the necessary transparency of approved prescribing and consumer information.

The current reliance on manual processes has resulted in a lack of clear information on the performance of the TGA and sponsors against existing evaluation milestones. This hinders the identification of areas for continuous improvement and the ability to collaborate on solutions.

The inability to link data between the TGA and other interrelated sections of the Department of Health is a significant deficiency. Initial targeted IT capital investment would inevitably save money. The value of achieving faster decisions for market authorisation has to take into account the timeframe for decisions on universal access through the PBS. Ensuring integrated data systems would improve monitoring, coordination and information sharing between sponsors and the government to achieve truly faster access to medicines for patients.

IT capability will enable appropriate KPIs and metrics for evaluation milestones to be established and provide greater predictability for government, patients and industry.
iv. Eliminating Unnecessary Red-Tape and Duplication

i. Pre-Submission Planning Stage

**Recommendation:**

Restructure the registration processes to allow rapid access to evaluation resources. If the current process of evaluation remains unchanged, then remove the existing pre-submission planning process and replace it with a notification scheme, such as the 10-day validation process used by the EU, to reduce regulatory burden and shorten timeframes for the approval of new medicines.

The Pre-submission Planning Form (PPF) process developed through the Business Process Reforms has been unsuccessful. In many instances the sponsor cannot commence the pre-submission process before receiving a full dossier for submission due to the overly burdensome information demands within the PPF.

Medicines Australia has been working continuously through the TGA/Industry working group since 2010 to resolve this issue, with no progress made after considerable industry efforts to reach a compromise. Medicines Australia members have reported that the earliest possible time to submit a PPF in Australia is within one month after the final dossier is available, effectively unnecessarily adding 14 weeks to the overall registration timeframe.

The level of information requested for planning purposes is unnecessary and creates a significant regulatory burden that compares very unfavourably with other pre-submission validation processes, such as the EU 10-day validation of a submitted dossier. In the US there is early engagement in the regulatory process between the sponsor and the FDA such that pre-submission validation is unnecessary.

As it is the practice of the TGA to only measure timeframes from submission of the actual dossier, the added time from inclusion of the pre-submission period results in a real timeframe that is at least three months longer than those of comparable agencies.

ii. Management of Post-Approval Changes

**Recommendation:**

Remove the existing preapproval processes for all variation applications and introduce post-approval variation processes that are commensurate with risk and aligned with those of the EU and the US.

The current 'risk-based' approach to regulation of post-approval variations does not reflect the actual risks according to the variation being requested.

Medicines Australia regards the requirement for all variations to be pre-approved as excessive and not commensurate with risk. Medicines Australia recommends that a notification system be implemented, possibly similar to the EU’s, whereby some changes that are not expected to reduce the quality, safety or efficacy of a medicine are notified to the agency on an annual basis.
However, changes that may affect quality, safety or efficacy should be appropriately assessed prior to implementation. Adoption of both processes would result in alignment to the level of risk associated with particular changes.

Given the current close alignment of Australia’s scientific requirements with those adopted by the European Medicines Agency, and assuming this scientific alignment will be retained, consideration could be given to adopting the requirements for post-marketing variations exemplified by the European approach to Type I and Type II variations.

This also applies to updates to the Product Information (PI) requiring the evaluation of clinical or nonclinical data. As soon as any evaluation of nonclinical or clinical data is required, the application is considered a Category 1 application and is subject to the same assessment timeframe as a New Chemical Entity application i.e. a maximum statutory limit of 255 working days. The TGA has introduced a Safety Change with Data category, but the scope of this is particularly limited. As a result, while the cost of different Category 1 applications differs significantly, minor changes to the PI take considerable unnecessary time to implement in Australia.

The post-approval variation process should align with existing global processes, in terms of target timelines for approval; classifications of the types of changes and supporting documentation requirements and a ‘do and tell system’ for minor variations on an annually reportable basis such as operates in the EU and US.

iii. Parallel Processing

**Recommendations:**

*Explore appropriate ways to further integrate regulatory and reimbursement processes to optimise parallel processing mechanisms to deliver faster access to subsidised medicines for Australian patients and reduce unnecessary red tape and duplication in current processes*

*Include vaccines in the scope of parallel processing*

Parallel processing, allows for concurrent evaluations of medicines by the TGA and the Pharmaceutical Benefits Advisory Committee (PBAC). The ability for a parallel process was introduced from 1 January 2011 as a measure under the Memorandum of Understanding (MOU) between the Commonwealth of Australia and Medicines Australia\(^\text{10}\).

These changes were seen as an important opportunity to gain efficiencies and improve time to access for Australian patients. Medicines Australia strongly recommends that any impact on parallel processing from reforms to regulatory or reimbursement processes be carefully considered, as this is an important feature of our system.

If international work sharing reforms are pursued, it is recommended that the Panel specifically address how approvals resulting from an overseas regulatory decision would be handled by the PBAC. If the TGA were to accept decisions on the basis of a reference decision, the ‘reference’ safety-efficacy evaluation would have to be made available for PBAC consideration. Retention of parallel processing for Australian regulatory and reimbursement evaluations, regardless of reforms to either set of processes, is critical to ensure timely access to medicines can be maintained and continually improved.

Medicines Australia also recommends that the parallel process be extended to encompass applications for vaccines reimbursement to improve access to vaccines for patients.

iv. Duplication in State and Territory Medicines Regulation

**Recommendation:**
Consolidate responsibility for medicines regulation into a single federal source

State and Territory regulated activities such as sample requirements, labelling provisions for signal headings, add increased burden without any benefit to public health and should be consolidated under the responsibility of the TGA.

A single body responsible for the regulation of medicines will enhance stakeholder understanding of requirements, benefit compliance and ensure the same standards apply across Australia. For example, the implementation of harmonised (nationally consistent) regulatory requirements for medicines labels represents a further opportunity for efficiency gains, and may help to improve quality use of medicines.

Having a number of different regulations and requirements for medicine labels in a number of different locations, including those set out in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) and related State and Territory Poisons Legislation is significantly burdensome to the pharmaceutical industry and results in duplication and cluttering of information on the medicine label. Cluttered and unclear labelling information further contributes to avoidable medication misadventure.11

v. Cost Recovery

**Recommendations:**

*The cost recovery structure of the TGA should be commensurate with the application type and the role of the regulator in the process.*

*The TGA should have the capacity to undertake independent work and provide public health information that is not cost-recovered from industry*

---

With a more flexible regulatory agency that allows for both sovereign decision making and the adoption of an overseas decision, there will need to be corresponding flexibility in fee structure. Fees should reflect the level of activity or service provided. Under a revised international work sharing model, the industry should not be charged fees for activities that have already been undertaken by overseas regulatory agencies such as manufacturing site audits, risk management plans or pharmacovigilance assessments.

Medicines Australia supports application fees that are based on the application type and the role of the regulator in the process (variable depending on level of service provided).

Medicines Australia further acknowledges that the TGA should have some capacity to undertake work unrelated to the evaluation of medicines and medical devices for sponsors. This requires a funding source outside of the current cost recovery model.

**vi. Clinical Trials**

**Recommendations:**

*Maintain the Australian CTN system in its present form*

*Launch the e-CTN/CTX platform as a priority*

Medicines Australia recommends that the Clinical Trial Notification (CTN) system should be maintained in its present form. An overwhelming majority of commercially sponsored clinical trials conducted in Australia are performed under the CTN system, with the alternative application pathway virtually unused. The current system eliminates unnecessary duplication and saves clinical trial sponsors in Australia a significant amount of time and money, which can be allocated to, among other things, other research projects.

However, even this successful system is in need of modernisation. Although it has a clear advantage for Australia in attracting global investment in clinical trials, it is hampered by being a manual system, at a time when clinical trial activity is in decline.

Moving from a paper-based to an electronic-based submission process for Clinical Trial Notification (and Exemption) forms would have two benefits. Firstly, it would reduce the time it takes for clinical trial sponsors to get the TGA’s approval to commence a clinical trial in Australia. Currently, the average approval time for CTN applications is three days, but accounting for postal and administrative delays, the process can take up to three weeks.

Secondly, an e-CTN platform that collected information from sponsors on a host of key performance metrics – such as the number of patients a site expects to recruit – would enable the TGA to provide reliable and accurate information on the performance and productivity of clinical trial sites in Australia. Among other things, this information could be used to benchmark the performance of Australian clinical trial sites against those in other countries, thus helping to identify areas for future reform.
CONCLUSION

Improved work sharing arrangements with other major regulators can provide tangible cost savings for industry and government.

Medicines Australia concludes that:

1. Adoption of expedited decisions from trusted overseas regulators will significantly reduce duplication of regulatory effort.
2. Redesigning local regulatory pathways to better manage the evaluation of medicines within Australia (such as fast, efficient generic evaluations and notification of post market variations) will also minimise unnecessary workload.
3. Local resources should be adapted to create fit-for-purpose evaluation pathways such as fast-track evaluations, conditional registrations, rolling submissions etc.
4. Updated and harmonised information technology will be critical to achieving success.

Up to 50% of Medicines Australia member companies’ applications for new chemical entities would achieve faster and more efficient registration decisions under these proposed reforms; thus reducing red-tape, reducing cost and resource burden and enabling faster access to safe and effective innovative medicines for Australians.

TGA revenue, on a fee-for-activity basis, will depend on the revised fee structures imposed. There are likely savings for Australian sponsors associated with local resources required to manage activities that would become streamlined with electronic processes and those that would be re-directed from local pre-market evaluation-related activities. There would be some additional savings to industry and TGA in production charges from publishing, submitting, distributing and storing printed dossiers.

The cost of maintaining registrations and all post-registration and pharmacovigilance activities would remain and could be further enhanced to support public health and safety and facilitate the adoption of new, alternate pre-market efforts.

This submission includes a number of areas of efficiency and advancement which we believe will benefit the Australian regulatory system for therapeutic goods. Once the panel has had sufficient time and input to develop a proposal for regulation in Australia we would expect to be part of the group to explore the proposed changes. Not only to ensure that Australians can continue to rely on a world class regulatory system but also to ensure that member companies have sufficient time and education to operate within the new system and therefore ensure there is no interruption in the access to innovative medicines, vaccines and devices in Australia.

In conclusion, Medicines Australia believes that targeted reform is required to evolve the Australian regulatory system to better reflect the global environment. Medicines Australia appeals to the Government to adopt the recommendations within this submission to simplify regulatory processes and harness international efficiencies where possible.
Submission to the Expert Review of Medicines and Medical Devices Regulation

Attachment A – Summary of Recommendations

January 2015
SUMMARY OF RECOMMENDATIONS

A summary of recommendations on Prescription Medicines for consideration as part of the Panel Review are presented in Table 1.

- Entries are grouped based on the key issues identified in the Discussion paper that contribute to ‘red tape’ including duplication; lack of flexibility; non risk-based assessments; complex and burdensome processes.

- For each entry the supporting rationale and any considerations on risk management to ensure the same level of protection of public health as existing arrangements is provided.

- Each recommendation is categorised into one or more of three groups as outlined below.
  - Categories indicate the level of complexity and need for legislative change representing short to longer term implementation timeframes.

**Category 1**  Changes to existing administrative or process related steps that do not require any legislative change to implement.

**Category 2**  Amendment or repeal of existing Legislative Instruments with potential need for preparation of a Regulatory Impact Statement (RIS) prior to implementation.

**Category 3**  Legislative change to Therapeutic Goods Act or Regulations or State/Territory or International collaboration requiring Inter-Governmental agreement.

Further context and responses to specific questions raised in the Discussion paper are provided in Attachment B.
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
</table>
| 1   | Retain the TGA as a regulator of therapeutic goods under a new framework that:  
    - Allows the adoption of expedited international decisions for breakthrough therapies to support early access for Australian patients and  
    - retains the ability of the Commonwealth of Australia to make sovereign decisions on marketing authorisations, in the interest of public health |  
    - Globalisation of drug development has resulted in increased standardisation of applications for innovative new medicines to support parallel global submissions with alignment of indications and conditions of use across major markets. This creates the opportunity for adoption of international decisions to deliver faster access for breakthrough therapies and facilitates increased collaboration between regulators reviewing common datasets in ‘real time’.  
    - Maintaining technical capability within the TGA is critical to enabling interactions with other regulators to realise the benefits of a worksharing model. It also ensures timely access to new medicines when Australia is the first or only market in the world to receive an application and can deliver an independent decision on approval.  
    - Independent decision making retains the flexibility for minor variations in approval conditions and ensures the relevance of divergent decisions between regulators e.g. EU and US on approvals or in response to safety signals can be appropriately assessed in the Australian context to protect public health. The right of industry to appeal decisions is also retained. |  
    - Access to breakthrough therapies for Australian patients in parallel with overseas jurisdictions will ensure equitable access and support optimal health outcomes. |  
    - Increased international collaboration will facilitate harmonised decision making and benefit post marketing risk assessment and signal detection to support early intervention and prevention of harm to patients |
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Establish criteria for a ‘trusted regulator’ operating to equivalent regulatory standards (e.g. Canada, EU and USA) to support worksharing based on the following principles:</td>
<td>- Increased international collaboration is a current global focus with the establishment of ICMRA (International Coalition of Medicines Regulatory Authorities). TGA is already engaged in multiple activities relating to generics, GMP and orphan drugs collaborating with Canada, EU, New Zealand, Singapore, Switzerland and US. These initiatives build confidence and lead to increasing alignment in regulatory decision making through common understanding. - Establishing transparent criteria for worksharing is pivotal to ensure public confidence in the quality, safety and efficacy of new medicines in Australia.</td>
<td>- Worksharing whilst retaining an independent approval decision, rather than blanket acceptance of overseas decisions, ensures that public health is protected. Consideration of new medicines in the context of the local environment and clinical practice best serves the interests of Australian patients. The right to appeal a decision is also retained.</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Description</td>
<td>Rationale</td>
<td>Risk Management</td>
<td>Category</td>
</tr>
<tr>
<td>-----</td>
<td>-------------</td>
<td>-----------</td>
<td>----------------</td>
<td>----------</td>
</tr>
</tbody>
</table>
| 3   | Develop a plan to create an evaluation pathway based on a worksharing model with 'trusted regulators' including Canada, EU and USA | • The regulatory framework in Australia currently aligns most closely with that in the EU, evidenced by multiple areas of collaboration including Orphan drugs, GMP and generics and adoption of the same approach for pharmacovigilance and risk management. The existing Mutual Recognition Agreement reflects the accord on common standards between the jurisdictions.  
• Similar collaborations also exist with other regulators such as Health Canada and FDA based on equivalent standards of medicine regulation and the general similarity of population demographics, disease burden and clinical practice across the major jurisdictions.  
• Evaluation pathways based on a worksharing model require the ability for agencies to share unredacted evaluation reports and Sponsor responses to maintain an appropriate level of benefit/risk assessment in the local context. In the EU, participation of Australia in the centralized and decentralized procedures (c.f. Norway and Iceland) could be an alternative worksharing option  
• Lack of involvement of Australian clinical trial sites during drug development may limit local clinical expertise leading to conservative decision making that may delay access to new innovative therapies. Access to the views of a larger pool of global clinical expertise will support maintenance of a ‘state of the art’ knowledge base to ensure optimum risk based decision making.  
• The EU centralized procedure facilitates access to medicines for a population of almost half a billion people through a process of collaborative decision making across 30 countries, whilst the US has a population of over 300 million. This provides public confidence that the same medicines can be safely made available in Australia without delays in access compared to overseas markets.  
• Transparent communication strategies can provide the relevant context for decisions that are divergent so that these are fully understood by the community and industry.  
• Worksharing whilst retaining an independent approval decision, rather than blanket acceptance of any overseas decisions, ensures that public health is protected by consideration of new medicines in the context of the local environment and clinical practice to best serve the interests of Australian patients. The right to appeal a decision is also retained. | | |
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Develop a process for assessment of new medicines through ‘worksharing’ rather than full evaluation in a parallel timeframe to a ‘trusted regulator’. The process should require minimal evaluation of quality and non-clinical data and focus on the relevance of the clinical data and risk management plan in the context of Australian clinical practice.</td>
<td>• Within the existing regulatory framework Category 2 applications can be made that rely on overseas evaluations. However the requirement for submission of reports from two independent regulators precludes parallel evaluation in Australia, thus delaying access to new medicines or lifecycle developments. As a consequence the process is rarely used. &lt;br&gt;• ICH technical requirements support harmonised quality and nonclinical data requirements as well as ongoing post-marketing benefit/risk assessment across the major regulators with Australia having aligned its current framework with that of the EU. &lt;br&gt;• Based on a common supply chain, review of quality and nonclinical evaluation reports from a ‘trusted regulator’ to confirm that the required standards have been applied should be sufficient, rather than full evaluation. In the case of differences between applications assessment only of items not previously evaluated should be undertaken. &lt;br&gt;• Clinical evaluation should focus on a risk assessment considering local clinical practice to ensure appropriate conditions of use to optimize the clinical benefit to patients. &lt;br&gt;• Assessment of risk management plans should not duplicate overseas evaluation but focus on the applicability of the global risk mitigation strategy to the Australian healthcare setting. Any differences in regulatory assessment of ‘risk’ should be fully evidence based to justify differences from international best practice and avoid unique Australian requirements that add red tape.</td>
<td>• Increased reliance on overseas quality and nonclinical evaluations based on the same dataset and standards of evaluation will not increase risk to public health. &lt;br&gt;• A simplified pathway for implementing lifecycle updates will ensure consistency with overseas approvals and equal access for Australian patients &lt;br&gt;• Evaluation of clinical data in the context of the local environment and clinical practice will ensure the decision on approval best serves the interests of Australian patients.</td>
<td>Category 2</td>
</tr>
<tr>
<td>No.</td>
<td>Description</td>
<td>Rationale</td>
<td>Risk Management</td>
<td>Category</td>
</tr>
<tr>
<td>-----</td>
<td>------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------</td>
<td>----------</td>
</tr>
</tbody>
</table>
| 5   | Implement a single Commonwealth regulatory framework for medicines that removes the additional burden of compliance with State and Territory requirements | • The same worksharing approach is appropriate for ongoing applications over the product lifecycle to ensure Australia patients benefit from ongoing product development  
• State and territory regulation creates additional complexity and regulatory burden that is difficult to navigate e.g. medicines labelling, sampling and AE reporting requirements in some states. This has the potential to prevent a harmonised standard for medicines across Australia resulting in red tape that is not in the interests of public health and a waste of industry time and resource.  
• Current requirements for medicines labeling outside of the control of the TGA, dictate the need for signal headings to occupy significant space on the front face of the labels. This impacts the space available to ensure the prominence of more critical information that would enhance the Quality Use of Medicines.  
• State based differences in AE reporting e.g. influenza vaccine reports can lead to delays in consolidation of country wide information important for optimal signal detection and creating additional complexity that is not in the interests of public health. Consolidation of all State based requirements under the responsibility of the TGA will avoid unnecessary duplication of effort. | • A single Australian wide approach will ensure consistency and compliance and enable industry to create optimal labels to support Quality use of Medicines and avoid potential confusion for patients travelling interstate | **High** |
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Amend the legislative framework to create additional approval pathways that allow patients early access and/or shorter evaluation timeframes for medicines in areas of high unmet medical need or significant medical innovation to include:</td>
<td>• Current inflexibility in approval pathways is driven by the regulatory framework available under the Therapeutic Goods Act. Revision is required to support a contemporary regulatory scheme adaptive to future developments in technology</td>
<td>• Experience in other jurisdictions has validated several early access/accelerated approval approaches that provide an appropriate balance between benefit and risk to ensure protection of public health</td>
<td>Red</td>
</tr>
<tr>
<td></td>
<td>a ‘priority evaluation/accelerated review’ scheme to shorten evaluation timeframes for therapies addressing an unmet need or offering significant medical innovation based on the criteria aligned with the EU or US breakthrough designation</td>
<td>• Expansion of options aligned with schemes available overseas will ensure Australian patients have the same level of access to innovative therapies as in other major jurisdictions such as the EU and USA where ‘fast-track/accelerated’ reviews are an option</td>
<td>• The existing requirements for ‘informed consent’ ensure an appropriate level of patient protection which is not enhanced by the administrative burden of the scheme.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a ‘rolling submission/adaptive pathway’ scheme for early access to promising new therapies still undergoing clinical development</td>
<td>• Early access schemes generally include ‘conditions’ aimed at protection of patient safety and requiring provision of additional data to confirm medicines continue to demonstrate a positive benefit-risk profile in clinical practice</td>
<td>• Better informed prescribers and patients will help to minimise risks through improved Quality Use of Medicines</td>
<td></td>
</tr>
<tr>
<td></td>
<td>a ‘conditional approval’ scheme based on the same criteria as in the EU for promising new therapies where confirmatory trials are planned/ongoing but have not yet completed</td>
<td>• Inclusion of similar conditions of registration in Australia as adopted overseas can ensure effective risk management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Simplify the administrative burden of the current SAS scheme by creating a single supply category for notifications through an electronic portal</td>
<td>• The current SAS scheme creates administrative burden for prescribers, particularly for the Category B scheme and simplification will facilitate early access for individual patients on a case by case basis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Improve Quality use of Medicines to minimise risks to patients from early access schemes, through improved presentation of product information, education and e-health initiatives that will enhance safety monitoring and signal detection to prevent harm to patients</td>
<td>• Early access requires appropriate oversight to prevent inappropriate use that may impact the longer term benefit/risk assessment by failing to deliver optimal clinical outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Description</td>
<td>Rationale</td>
<td>Risk Management</td>
<td>Category</td>
</tr>
<tr>
<td>-----</td>
<td>-------------</td>
<td>-----------</td>
<td>-----------------</td>
<td>----------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prescribing (Product Information -PI) and patient information (Consumer Medicines Information - CMI) contain important information to support the appropriate use of Medicines. However the current PI format does not support the user readily identify critical information such as indications, dosing, contra-indication and warnings reducing its value as a risk mitigation tool.</td>
<td>Easier access to critical prescribing information will enhance Quality use of Medicines to better protect patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Revising the format of Prescriber and Consumer Information documents to prioritise the presentation of information critical to safe use and more readily align with formats used in the EU and US</td>
<td>Raising community and health professional awareness of the importance of safety monitoring of medicines through an educational campaign will support quality use of medicines and encourage reporting to ensure early signal detection</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Improved e-health records that hold real world outcome data will support interrogation of records to identify early safety signals enabling a rapid intervention to mitigate any risks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Align data exclusivity periods with international best practice and ensure early access does not impact IP rights</td>
<td>The competitiveness of innovator companies in Australia is impacted by the lack of comparable IP protection compared to overseas jurisdictions such as the EU and USA.</td>
<td>Provision of appropriate incentives for industry will ensure Australian patients benefit from ongoing R&amp;D and that Australia remains an attractive market for investment</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Review the options for amending the Therapeutic Goods Act and Regulations to support more timely updates, to ensure the regulatory framework remains fit for purpose in the light on ongoing medical innovation</td>
<td>The increased understanding of genetics together with rapid developments in biotechnology and digital technologies e.g. 3D printing of hip replacements and health apps, increasingly lends itself towards personalised medicines and holistic solutions for disease management incorporating diagnostic tests, medicines and health apps.</td>
<td>Creating the same opportunities for Australian patients to benefit from medical innovation available overseas ensures equitable healthcare options and optimal clinical outcomes.</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Description</td>
<td>Rationale</td>
<td>Risk Management</td>
<td>Category</td>
</tr>
<tr>
<td>-----</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------</td>
<td></td>
</tr>
</tbody>
</table>
| 11  | Define a post-approval lifecycle framework for quality variations aligned with that in the EU that reduces the submission burden for industry and establishes activity based timelines for evaluation | • The current requirements for prior approval of all quality changes do not reflect an appropriate risk based model and is an unintended consequence of the existing legislative instruments  
• Extending the existing alignment with EU quality standards in the pre-approval setting to the post approval setting will reduce the need to create Australian specific packages, support annual reporting of minor updates and facilitate worksharing.  
• Elimination of Australian specific requirements creates flexibility for manufacturing plants needing to accommodate global supply needs and reduces the risk of medicines shortages due to unique market requirements | • Long standing experience of annual reporting schemes in EU and US support adoption of the same approach in Australia without any decrease in quality standards or risk to public health |                                                                                           |
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
</table>
| 12  | Define a post-approval lifecycle framework for clinical variations that supports rapid implementation of safety updates, maintains currency of clinical information to reflect best practice and reduces the submission burden for industry and establishes activity based timelines for evaluation                                                                                                           | - Changes to the Act are required to support rapid implementation of safety related changes via a notification process which does not require an approval decision, as has been undertaken in the past. Significant additional red tape was created when standard processes used by both the TGA and industry were found not to be in accordance with the requirements of the Act. The inability to update the Act in a timely manner resulted in adoption of a sub-optimal solution neither benefitting industry or the TGA.  
- Current life cycle management of clinical updates beyond safety related requests require a Category 1 application regardless of the level of information being considered. This results in evaluation timeframes significantly longer than in the EU or US resulting in misalignment of global labelling information whilst the review is ongoing  
- Changes to the Act are required to define specific sub-categories of applications with activity based timeframes. Models in other jurisdictions include options for 30, 60 or 90 day reviews in the EU dependent on the nature of the changes being made.                                                                 | - Ability to rapidly implement safety changes is in the interests of public health.  
- Review of clinical updates in timeframes more aligned with international best practice ensures there is no delay for Australian patients to benefit from life cycle developments such as new indications or to implement labelling updates to mitigate risks  
- Out of date prescribing and consumer information does not support Quality Use of Medicines and can impact patient care, thus the availability of up to date information is a shared imperative of industry, clinicians and the TGA                                                                                           |          |
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
</table>
| 13  | Establish a joint agency/industry working party to recommend changes to all guidance and legislative instruments that include unique Australian standards that are barriers to acceptance of decisions of other major regulators and/or increase regulatory burden due to administrative complexity | - Multiple standards currently applied add red tape and administrative burden and reduce the flexibility of the evaluation process. Examples include Module 1 requirements including GMP and DMF processes; mandatory requirements for Category 1 applications and the Australian specific annex for RMPs. Simplification of requirements and elimination of Australian specific requirements will save time and resource.  
- Elimination of Australian specific requirements reduces the risk of medicines shortages due to unique market requirements | - Application of ICH harmonized standards aligned with other jurisdictions support an appropriate level of rigor for benefit/risk assessment without undermining patient safety  
- The similarity of population demographics, disease burden and clinical practice across major jurisdictions and historical experience support acceptance of overseas data without compromising medicines safety | Category 1 |
<p>| 14  | Define Regulator Performance Assessment Measures that include stakeholder engagement activities with regulated entities including training and education, to ensure appropriate risk-based regulation is applied to the sector and the impacts of regulation are understood | - Lack of awareness of operational aspects of managing a global supply chain can result in impractical proposals for regulation that are a burden to industry e.g. recent packaging and labelling review and annual testing of biologicals. | - A level of regulation appropriate to risk ensures protection of public health and maximizes the resources available for the development of new medicines | Category 1 |</p>
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• Disproportionate regulation can reduce industry investment in R&amp;D to develop innovative new medicine and significant time and resource can be wasted in order to move forward from entrenched positions to find a practical solution. • Open and transparent dealings with regulated entities is critical to ensure impacts of regulation are understood and aligns with the regulator performance assessment framework</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Eliminate the existing pre-submission planning process and replace with a notification scheme, aligned with international best practice, to reduce regulatory burden and shorten timeframes for approval of new medicines</td>
<td>• The current pre-submission process can delay the start of evaluation of new medicines in Australia by 2-3 months due to the requirement for essentially 'complete' Module 2 documentation that is contained in the final submission. This level of information is not required by any comparable regulator for planning purposes and is a significant regulatory burden • The mandatory requirements include unique Australian requirements that can result in additional cost and time delays to generate the necessary data • Inflexibility in the process requires a completely new pre-submission application to be initiated, resulting in up to 3 months delay to start of evaluation, if deficiencies are identified, rather than allowing corrections within a short timeframe as in other jurisdictions</td>
<td>• Removal of an administrative step has no impact on public health</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Improve certainty on approvability by re-engineering the evaluation process to support parallel processing of PBS submissions and more timely access to new medicines</td>
<td>• The lack of an integrated benefit risk assessment early in the current process leads to uncertainty around the final regulatory decision which impacts business planning and parallel PBS submissions.</td>
<td>• Improvement in aligning the regulatory and reimbursement process steps has the potential to positively impact timely availability of new medicines or lifecycle development to the benefit of public health</td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Description</td>
<td>Rationale</td>
<td>Risk Management</td>
<td>Category</td>
</tr>
<tr>
<td>-----</td>
<td>-----------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>----------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The heavy reliance on external clinical evaluators can result in delays due to poor quality assessments needing to be corrected by TGA staff. An ability to reduce reliance on contract clinical evaluation resource would enhance timeliness and consistency of evaluations.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regulatory process steps should be integrated with the timelines of the reimbursement process to avoid delays due to misalignment e.g. lack of Delegates Overview for PBS ‘cut-off’ date.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Limitations in available expertise, especially clinical external evaluators and advisory committee members, can result in unexpected decisions that do not align with international best practice.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>The result is lengthy appeal processes to obtain the same outcomes as overseas. This lack of predictability reduces the attractiveness of Australia as a country for R&amp;D investment and does not meet the operational benchmark of other regulators.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Restructure the TGA to deliver integrated premarket assessment capabilities and eliminate silos across Offices that can add red tape and uncertainty on approvals for Sponsors</td>
<td>Current evaluation responsibilities are split between the Office of Market Authorisation, Office of Scientific Evaluation and Office of Product Review which can result Sponsors needing to co-ordinate across the departments to avoid delays in finalising approvals due to operational ‘silos’ that create additional red tape.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>A comprehensive assessment of benefit risk requires an integrated approach to achieve the best outcome that ensures protection of public health and timely access to innovative new medicines.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>Description</td>
<td>Rationale</td>
<td>Risk Management</td>
<td>Category</td>
</tr>
<tr>
<td>-----</td>
<td>-------------</td>
<td>-----------</td>
<td>----------------</td>
<td>----------</td>
</tr>
</tbody>
</table>
| 18  | Re-define the terms of reference of Advisory Committees to ensure appropriate expertise is trained on regulatory process, adds value and provides advice aligning with the 'Industry Innovation and Competitiveness agenda ' on risk assessment thus avoiding additional requirements vs international best practice | - The role of the current TGA advisory committees e.g. ACSOV, ACSOM, ACPM should be reassessed to increase transparency and ensure that experts with the relevant disease and/or product specific knowledge e.g. clinical trials/practice experience are available and advice provided aligns with standard regulatory practice. There is a lack of clarity on the selection and training on regulatory process of advisory committee members.  
- Advice that includes burdensome and unnecessary recommendations for additional data that does not align with international best practice, creates 'red tape' and adds to Sponsor uncertainty on approval, even if subsequently advice is disregarded by the Delegate. | - Worksharing arrangements will support access to a broad range of overseas clinical expertise that can support local clinical experts in local risk assessment |  |
| 19  | Improve TGA IT-systems to establish full e-business capability, enhance inter-departmental co-operation within the DoH, eliminate green tape, streamline communications and processes and establish appropriate KPIs and metrics for evaluation milestones | - Elimination of paper will reduce submission costs and facilitate filings in parallel with other global markets  
- Reduced manual processing will allow resources to be focused on technical assessments of quality, safety and efficacy to ensure timely access to new medicines. This ensures better use of user fees for the benefit of public health.  
- Adoption of E2B capability and the ability to link to 'real world' data sources such as e-health records will enhance pharmacovigilance activities. This will enable resources to be focused on assessment of risk and signal detection to protect public health rather than manual, burdensome, administrative processes | - Improvements to administrative and process steps do not impact the quality of the benefit/risk assessment but may positively impact the speed of access to new innovative medicines  
- Use of technology to assist in the management of post marketing surveillance activities will enhance the ability to protect public health through faster identification, analysis and communication of risks |  |
## Attachment A: Recommendations

### January 2015

**Review of Medicines and Medical Devices Regulation - Response to Discussion Paper**

<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>17</td>
<td>Implementation of an electronic portal for Clinical Trial Notification (CTN) lodgement would further enhance speed of receipt of acknowledgement would support innovation and competitiveness. This would encourage investment in the conduct of R&amp;D in Australia with overall benefits for the broader economy</td>
<td>Local clinical experience gained through involvement in clinical trials of innovative new medicines supports optimal Quality Use of Medicines at product launch and enables TGA and PBAC to access experts that can provide insights relevant to use in local clinical practice</td>
<td>Improved transparency of regulator performance will allow optimal benchmarking of the timeliness of approvals in Australia vs other jurisdictions to ensure timely access for Australian patients</td>
<td><strong>Category</strong></td>
</tr>
<tr>
<td></td>
<td>An electronic workflow will enable Sponsors to monitor progress of applications in real time and reduce administrative burden from handling enquiries that can detract from evaluation time.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A secure e-communication network will facilitate agency-Sponsor interactions and eliminate delays due to reliance on mail delivery which can impact business planning and innovation e.g. delays in receipt of a CTN acknowledgement to support initiation of a clinical trial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Connecting interrelated sections of the DoH to enhance communication to support faster decisions on access to medicines will support innovation and ensure the competitiveness of the Australian industry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Availability of information on milestone metrics will enable issues to be identified to provide greater transparency and predictability for industry and facilitate continuous improvement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Eliminate the need for inclusion of prescribing information leaflets in injectable medicines</td>
<td>Electronic means of distribution of prescribing and consumer medicines information are readily available to reduce green tape. Printing and replacement of out of date leaflets is a significant cost and burden to industry that decreases the investment available for innovation.</td>
<td>Access to the most up to date prescribing and consumer information in a format that allows easy navigation to identify critical information improves patient safety through optimal Quality Use of Medicines</td>
<td><strong>Category</strong></td>
</tr>
<tr>
<td>No.</td>
<td>Description</td>
<td>Rationale</td>
<td>Risk Management</td>
<td>Category</td>
</tr>
<tr>
<td>-----</td>
<td>-----------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------</td>
</tr>
</tbody>
</table>
| 21  | Improve the TGA website to ensure regulatory requirements are transparent to assist business planning and changes are optimally communicated to stakeholders | - For effective business planning access to up to date guidance on regulatory requirements is critical. Visibility of plans to implement changes and effective ‘alerts’ when revised processes are implemented avoids wasted time and resource and prevents submission delays  
- Appropriate transition periods should apply when changes or new requirements are implemented to avoid unnecessary burden that may delay access to medicines | - Ensuring the expectations of the regulator are met through clear and transparent communication of requirements will support industry in delivering complete and high quality applications to support early access to innovative new medicines | **Green** |
### OTHER RECOMMENDATIONS

<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
</table>
| 22  | Revise the fee structure for regulatory activities to deliver | • Worksharing arrangements when implemented will reduce evaluation time and hence under cost recovery lower fees should be incurred  
• To undertake its role to protect public health and retain its status as an internationally recognized regulator the TGA should have capability to undertake work unrelated to evaluation that should be funded outside of the cost recovery model  
• Current fee waivers for orphan drugs or annual fees based on low turnover are the primary means of support for small and medium enterprises seeking registrations for new products. Sponsors ineligible for waivers thus essentially pay higher fees to ensure sufficient revenue for TGA to recover costs of evaluations.  
• To encourage innovation access to financial and other technical support from sources outside of the cost recovery model, similar to schemes established in the EU, should be established  
• Recovery of fees for services undertaken should not impact the overall efficiency of the agency  
• Maintaining a world class regulator and ‘fit for purpose’ regulatory scheme warrants investment in time and resource for activities outside of evaluation that  
• Supporting innovation will help to bring new therapeutic options to patients to the benefit of public health | | Category | |
|     | • reduced fees for evaluations undertaken under a worksharing model with additional efficiencies from increased IT functionality  
• enable the TGA to partake in activities outside of evaluation that support future developments in regulation that are in the interests of public health  
• support small and medium enterprises to deliver innovative new products to the Australian public | | | |
| 23  | Establish an integrated process for evaluation of registration and scheduling applications under the responsibility of the TGA to reduce red tape and stimulate innovation to support Rx to OTC switch applications by | • The current scheduling arrangements for medicines are inefficient and should be fully integrated within the medicines evaluation process under the responsibility of the TGA. For rescheduling applications if external expertise is required, adoption of a committee structure similar to existing committees e.g. ACPM would be an appropriate model. | | Category | |
|     | • creating a more efficient process with shorter timeframes for a final approval  
• allowing advertising of Schedule 3 Pharmacist only Medicines with safeguards for exceptions if required | | | |
<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
<th>Rationale</th>
<th>Risk Management</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>Create a model support by codes of practice and guidelines for prescription medicine Sponsors to communicate directly with patients to support Quality Use of Medicines, considering the current global reach of the internet as a source of unvalidated consumer information</td>
<td>• Medicines Australia does not support advertising of prescription medicines to consumers. However access to information on the internet is readily available to the Australian public and developments in technology will continue to expand the ease of communication including through patient blogs/forums with global reach</td>
<td>• The availability of validated information relevant to Australian clinical practice will help to ensure patients receive the optimal information to support Quality Use of Medicines.</td>
<td>✓</td>
</tr>
<tr>
<td>25</td>
<td>Ensure any ‘red tape’ reduction in TGA operational activities do not come at the cost of increased red tape by other government agencies that operate with less transparency than the TGA and with no overall benefit to early access to medicines and the competitiveness of industry in Australia</td>
<td>• Acceptance of worksharing arrangements in decision making by the TGA should not result in other agencies within the DoH duplicating evaluation of quality, safety and efficacy.</td>
<td>• Improved collaboration across departments will increase transparency of operations to industry, prevent working in silos and reduce red tape.</td>
<td>✓</td>
</tr>
</tbody>
</table>
Submission to the Expert Review of Medicines and Medical Devices Regulation

Attachment B – Responses to Discussion Paper Questions for Consideration

January 2015
CHAPTER FOUR: PRESCRIPTION MEDICINES

Theme 1: Duplication of regulatory processes

Theme 2: Lack of flexibility required to facilitate early access to innovative products

Theme 3: Regulatory requirements are not commensurate with risk

Theme 4: Complex regulatory framework

Theme 5: Overly burdensome processes

CHAPTER FIVE: REGULATION OF BIOSIMILARS

CHAPTER SIX: OTC MEDICINES

CHAPTER SEVEN: MEDICAL DEVICES

CHAPTER EIGHT: FRAMEWORK FOR ADVERTISING THERAPEUTIC GOODS
CHAPTER FOUR: PRESCRIPTION MEDICINES

Theme 1: Duplication of regulatory processes

ISSUE 1 – HOW MIGHT A TRUSTED OVERSEAS REGULATOR BE DEFINED?

What options are available for determining ‘trusted overseas regulators’?

A regulatory authority could be considered a trusted ‘overseas’ regulator if they meet the following criteria:

- accepts the electronic Common Technical Document ((e)CTD) developed by the International Conference on Harmonisation (ICH);
- regulates for a population demographic representative of the Australian population;
- has a technical capability to evaluate and make an independent regulatory decision in accordance with ICH guidelines;
- communicates and prepares evaluation reports in the English language; and
- provides access to full evaluation reports in a timely manner.

Under these criteria, the following would represent a review by a trusted overseas regulator:

- Committee for Medicinal Products for Human Use (CHMP) Opinion under the centralised procedure co-ordinated by the European Medicines Agency (EMA); or
- Evaluation reports prepared by the United Kingdom (UK), United States of America (USA) and Canada.

If a criteria based approach were to be adopted, what criteria should apply in determining whether or not an overseas regulator is trusted?

- Accepts ICH criteria for (e)CTD and undertakes full evaluation of the data; or
- Has an existing relationship of trust and collaboration with the Australian Therapeutic Goods Administration (TGA).

If the TGA receives an application for registration of an NCE in Australia and the NCE has been approved by one trusted overseas regulator but rejected by another, should the submission be assessed by the TGA? If not, why not?

Yes. The TGA is an independent regulatory authority and has the capacity to make an assessment and decision made on local considerations, which should be utilised under such circumstances.

Irrespective of the shape of a restructured regulatory system, flow on, indirect, unintended and intended consequences will need to be thoroughly assessed as part of the review’s consideration, including (but not limited to) consideration of the following issues:

- Patent protection is country specific and will need to be considered before granting automatic/internationally assisted approvals. A mechanism would be required to ensure that the adoption of an overseas approval did not infringe local patent or data protection provisions, as there are frequently differences in IP across jurisdictions.1

---

1 Medicines Australia recommends that the term of data exclusivity in Australia be extended from five to 12 years for all new medicines and vaccines to more closely align with data exclusivity provisions in the US, EU, Japan, Canada and other developed countries.
However, revisions to the regulatory framework would also provide an opportunity to enhance patent notification in Australia to fully meet the terms of the USFTA.

- Biosimilar legislation, including naming legislation, differs across the world, so depending on the reference country used, different standards would apply. Comparator products would not necessarily be approved for marketing in Australia, although this is currently a fundamental requirement in the Australian regulatory paradigm.

**What other options would ensure that the health and safety of Australian consumers is protected?**

Automatic adoption of a trusted international decision should be at the request of the sponsor and should follow an expedited process with specific acceptance criteria. This model would be appropriate where the sponsor and the Australian regulator are satisfied that the international decision has adequately accounted for all potential benefits and risks that are relevant to the Australian population, so that public health and safety would not be compromised. The sovereign decision to accept the approval would remain with the Commonwealth of Australia through the TGA.

Expanded work sharing should be established that enables parallel submission with overseas regulators, with the retention of local decision-making authority by the TGA. Under such a proposal, two or more partner regulators (such as FDA, EMA and TGA) would share the evaluation of a single submission such that the assessments are conducted by one regulator on behalf of the others and the assessment is shared across all regulators in the arrangement. The approval decision would still be made by the TGA but can be granted at the same time as the other regulators. This would enable Australian patients to have access to medicines at the same time as patients in the US or the EU.

*If a trusted overseas regulator rejects an application for marketing of a medicine for the same indications for which that medicine has been registered in Australia, should this spark a review by the TGA?*

Depending on the timing and circumstances of the TGA decision, a review might be warranted but the ability of the TGA to come to an independent decision must be preserved.

**ISSUE 2 – IS THERE GOOD REASON FOR AUSTRALIA TO IMPOSE ADDITIONAL REQUIREMENTS?**

*Should the TGA approve the registration of a medicine on the ARTG on the basis that it has been approved for the same indications by a trusted overseas regulator? If not, why not?*

No. The approval of new medicines must be made following an independent risk benefit assessment by the TGA in the context of Australian clinical practice.

The sponsor and the Australian regulator must be satisfied that the international decision has adequately accounted for all potential benefits and risks that are relevant to the Australian population, so that public health and safety would not be compromised.

However, under the circumstance where a medicine and/or a specific indication have been approved in a foreign jurisdiction of a trusted regulator for a significant number of years, a registration could be automatically approved in Australia.
What value do you believe an assessment by the TGA adds in cases where such an assessment has already been undertaken by a trusted overseas regulator?

Australian context is considered meaning approval can be broader to fit with local clinical practice and Australian healthcare environment.

Establishes a knowledge base required for effective post-marketing monitoring of risk.

Are there aspects of safety, quality or efficacy that need to be considered in the Australian context? If so, what aspects?

- Potentially different clinical practice in Australia to other jurisdictions and implications for clinical efficacy and safety due to disease burden e.g. melanoma.
- Elements of quality e.g. Australian broad climatic conditions and supply chain requirements.
- Australian de novo applications by e.g. Australian biotech industry, generic companies require local evaluation capability.

Would consideration of these aspects necessitate a full assessment of the entire application by the TGA? If so, why?

Not all applications are submitted to overseas regulators in which case full assessment is required. For other considerations, full or a limited subset of data may need to be assessed.

Should sponsors of medicines that have been approved by a trusted overseas regulator have to submit an Australian specific Module 1 of the CTD to the TGA for assessment? If not, why not?

Yes.

Certain administrative data is required for efficient application management and subsequent product registration.

If Australia-specific packaging and labelling is to remain, details will be needed in Module 1.

However, there is certainly potential for simplification of the requirements for Module 1.

Even for a full TGA assessment, it can be substantially abbreviated if red tape is cut as suggested:

<table>
<thead>
<tr>
<th>Module 1 requirements</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 Letter of Application</td>
<td>Yes</td>
</tr>
<tr>
<td>1.0.0 Electronic lodgement cover sheet</td>
<td>No (red tape)</td>
</tr>
<tr>
<td>1.0.1 Letter of application</td>
<td>Yes</td>
</tr>
<tr>
<td>1.0.2 Responses to questions</td>
<td>Yes</td>
</tr>
<tr>
<td>1.1 Comprehensive Table of Contents</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2 Application forms</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2.1 Application form</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2.2 Pre-Submission Details</td>
<td>No (red tape)</td>
</tr>
<tr>
<td>1.2.3 Patent Certification</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3 Medicine information documents, packaging and labelling</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3.1 Proposed Australian product information and package insert</td>
<td>Yes (pack insert redundant)</td>
</tr>
<tr>
<td>1.3.2 Proposed Australian consumer medicine information</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3.3 Therapeutic goods and use of human embryos or human embryonic stem cells or material derived from them</td>
<td>No</td>
</tr>
<tr>
<td>1.3.4 Label mock-ups and specimens</td>
<td>Yes</td>
</tr>
</tbody>
</table>
What do you see as the risks and benefits of not requiring sponsors to submit an Australian specific Module 1?

There has to be at least some detail in Module 1 to support submission management, however, Sponsors would benefit greatly from not having to supply the red tape, redundant or duplicative requirements. The amount of reduction of Module 1 following removal of these elements depends on if or how much of the “trusted regulator” decision is adopted. Transition to eCTD facilitates removal of redundant information from Module 1.

Without having specific medicine information (PI, CMI, label), there is a risk that the medicine may not be appropriately positioned for the Australian healthcare environment. Without information on labelling for example, lifecycle management of future variations would be difficult as there would be no baseline comparison.
What would be the likely quantum of savings to industry per application, if Australia was to accept assessments of trusted overseas regulators, with or without a requirement to submit an Australian specific Module 1 of the CTD to the TGA for assessment?

Due to the diversity of arrangements by which dossiers are prepared by different Sponsors, estimating potential savings per application is difficult. However, for Australian affiliates of global organisations Modules 2-5 are already available based on work done to prepare the EU submission and creation of the local Module 1 is a routine process.

However, if assessment reports from overseas regulators were to significantly influence future TGA evaluations, it is expected that the Australian evaluation timeline would be significantly reduced (from the current 255 working days), and for TGA evaluation fees to be significantly reduced from current levels.

Module 1 preparation time in Australia is consumed largely by the development of Australian-preferred (text and formatting) Product Information and Consumer Medicine Information documents and risk management documents including the current requirements for an Australian Specific Annex. Unique Australian requirements such as bio-summary forms, GMP pre-clearances and DMF/CEP letters of access if required can also take considerable time and resource both locally and globally.

Would such an approach:

Result in delayed access to new medicines by the Australian public? If not, why not? If yes, are there strategies that could be put in place to prevent this from occurring?

Potentially. Many companies currently achieve an approval in Australia earlier than in Europe. Some indications in Australia (e.g. for oncology products) are not approved at all in the US due to different regulatory endpoints for study design. Australia needs to retain the capacity for rapid, fit-for-purpose assessment.

The benefits of replacing the Australian registration decision making process to one that relies entirely on adoption of international decisions would be entirely negated if this approach resulted in a product that could not be effectively commercialised in Australia.

Therefore, Medicines Australia recommends expanded work sharing with overseas regulators with the retention local decision-making authority by the TGA on the basis of an assessment of the opportunities (efficiencies) and risks of this and other models of regulatory reform.

Key consequences of relying solely on an automatic adoption model include:

- Delayed registration timeframes and delayed market access;
- Inability to tailor applications to the Australian population and a loss of ability to influence post approval risk management in the Australian context;
- Timeframes or outputs from international regulators that do not meet the needs of the Australian reimbursement system;
- Lack of regional leader in regulatory sciences, particularly Asia Pacific region;
- Reduction in expertise and resources within the TGA, reducing its ability to maintain the current standard of evaluation of medicine applications and timely entry to Asia Pacific markets;
- Under informed, under resourced regulator not responsible for local evaluations would be less able to address ongoing regulatory issues (pharmacovigilance; recalls; shortages; adverse events);
Attachment B – Responses to Questions for Consideration

- Loss of appeal mechanisms with the acceptance of another agency decision (loss of review by regulators, courts, tribunals) will create an environment that does not optimise the labelling and conditions of use for the Australian market and may impact overall patient outcomes;

- Potential increased liability risk for sponsors if automatically adopted decisions do not address specific local issues e.g. differences in clinical practice/availability of medications that result in increased risk to Australian patients;

- In the longer term, this type of model could discourage Australian manufacture and innovation and reduce flexibility and independence in Australia.

**Undermine TGA-PBAC parallel processing mechanisms? If so, how might this be managed?**

Waiting until approval by a ‘trusted overseas regulator’ is granted will potentially undermine the current TGA-PBAC parallel process. Companies generally time their PBAC submission so that the Committee receives the TGA Delegate’s Overview ahead of the PBAC meeting. If the PBAC does not receive this, the application for reimbursement is typically deferred.

Any new regulatory framework that relies on the acceptance of an assessment of a trusted overseas regulator must include a mechanism to assist the interplay between the TGA and PBAC processes.

Greater coordination between TGA Advisory Committee and PBAC meetings would also reduce the lag time between the TGA Delegate’s Overview being issued and the PBAC meeting. Better integration and coordination of TGA and PBAC operations would enable industry to take full advantage of the TGA-PBAC parallel process.

A joint TGA-PBAC pre-submission advice framework would allow for better utilisation of parallel TGA-PBAC processing and possibly Managed Entry Scheme.

It must be acknowledged that where a potential for expedited approvals is being considered, there needs to be mechanisms in place to facilitate acceleration in parallel with reimbursement decisions, without further undue duplication of evaluation.

Unless the PBAC takes over the role of regulator, it can’t be managed well as the regulatory knowledge and assessment will no longer reflect Australian clinical practice.

**ISSUE 3 – WHAT IS MEANT BY PRODUCT APPROVAL?**

*Should a change to a medicine that has been approved by a trusted overseas regulator necessitate a further assessment by the TGA in circumstances where that change may impact safety, quality or efficacy? If not, why not?*

Yes.

In some cases medicines have different technical details for different markets, so the trusted regulator might not have the same product. Clinical practice might also vary between jurisdictions.
If yes, should the assessment by the TGA be limited only to those aspects of the application that are impacted by the change?

Where appropriate this approach should be used, however the TGA’s overall capability to complete an assessment should not be reduced by limiting evaluation.

If Australia was to accept approvals of medicines by trusted overseas regulators, should this include conditional/provisional approvals? If not, why not?

Australia has for decades made an independent decision based on available evidence. This has not, but should in future embrace options for conditional/provisional approvals.

If yes, should the marketing conditions/provisions imposed by the trusted overseas regulator also apply in Australia? If not, why not?

Yes, however many post-marketing commitments need not actually be performed in Australia and reliance on data from overseas markets with comparable demographics is appropriate.

Should there be capacity for Australia to impose its own conditions, either in addition to, or in place of, those imposed by the trusted overseas regulator and if so, why?

Not unless an Australian-specific clinical context has been identified.

Theme 2: Lack of flexibility required to facilitate early access to innovative products

Should Australia introduce an accelerated approval program(s)? What are the potential risks and benefits of such programs and how might the risks be managed and the benefits maximised?

In considering accelerated approvals both ‘priority review’ (reduced evaluation timeframe) and ‘conditional’ approval in the absence of a full data set should be considered.

Patients with serious or life-threatening conditions with limited or no therapeutic options require early access to innovative medicines to address their unmet medical need. In addition, technological innovations should be eligible for and accelerated approval process e.g. devices including in vitro diagnostic tests or delivery systems that show a significant improvement in patient outcomes either through mitigating a risk or enhancing quality use of medicines.

Risks of early access relate to immature safety and efficacy data sets (Phase II) that may evolve to indicate an ineffective or unsafe medicine. These risks can be mitigated using the same approach as in other markets in which early access schemes have existed and that have been validated over many years.

- Legislative provision for ‘conditional registration’ c.f. EU/NZ provisional consent that specifies a period of validity (1 year in the EU) and requires ongoing submission of data to convert to full registration.
- Use of ‘conditions of registration’ that require increased vigilance for signal detections.
- Limit access through ‘protocol’ or ‘qualified’ prescriber schemes.
- For products with Phase III data under regulatory evaluation, for enabling earlier access to patients, consideration of an access scheme c.f. French ATU that allows broad access under controlled conditions at limited sites.
If Australia were to introduce an accelerated approval program:

**Should there be a single pathway (as per the EU model) or multiple pathways (as per the US approach) to apply?**

Flexibility to support multiple pathways is required to accommodate different situations for example:

- Rolling submissions to support priority review; and
- Conditional approvals to support early access or adaptive pathways.

**What eligibility criteria should apply to the pathway(s)? That is, under what circumstances could a sponsor apply for accelerated approval of an NCE?**

Global alignment with other regulators will facilitate sharing of experience under the same circumstances e.g. serious debilitating condition with unmet medical need, or a life threatening condition.

**If medicines were to be provisionally approved, based on more limited clinical data than is traditionally required for a full approval:**

**What additional requirements, if any, might be appropriate to alert prescribers and/or consumers to the provisional approval and its implications?**

- New category of registration reflected in legislation e.g. AUST C (conditional registration).
- Statement in the Product Information (PI) and Consumer Medicines Information (CMI) c.f. EU Summary of Product Characteristics (SmPC) necessary for healthcare professionals (HCP) and patients to ensure the scope of the approval is understood and that if confirmatory data is not positive that access may need to be removed (Note: the PI and CMI need to be utilised much more effectively as accessible electronic documents available to provide continuously current information).
- Symbol on packaging to identify product is not subject to full approval and requires additional vigilance for safety monitoring.

**What requirements would need to be in place to manage withdrawal of the medicine from the Australian market if safety or efficacy concerns emerged?**

- Standard Dear Health Care Professional Letters;
- Recall options;
- Additionally, agreements should be put in place to enable TGA to access/share EU/US safety databases, to enable interrogation of real world data and facilitate post marketing surveillance and signal detection.
Theme 3: Regulatory requirements are not commensurate with risk

ISSUE 1 – APPROVAL OF VARIATIONS

Should Australia adopt a risk-based regime for variations, which allows notifications and/or annual reporting for changes that are at low risk of impacting the quality, safety or efficacy of the product? If not, why not?

If yes, what might such a regime look like? How might notification/reporting procedures be designed so as to minimise burden on sponsors?

Yes. Medicines Australia supports a simplification of post marketing activities to manage a product lifecycle modelled on existing overseas frameworks that provide industry with the necessary flexibility to implement minor updates without needing a prior regulatory review.

The adoption of an annual reporting system would reduce the regulatory burden as the changes to the Chemistry, Manufacturing and Control (CMC) information would have low risk from a quality and regulatory perspective and would allow the sponsor to continue to provide medicines in an expeditious manner.

The US FDA guidance on acceptable annual reportable changes or an EU-like, 'tell, wait, do' notification system should be considered.

Alignment with the scheme in the EU or US would enable EU/US submission packages to be utilised with minimal reworking for TGA.

ISSUE 2 – APPROVAL PROCESSES FOR MINOR VARIATIONS TO A MEDICINE FOR THE PURPOSE OF EXPORT

How might the process for minor variations for export-only medicines be streamlined so as to facilitate more timely access to export opportunities without compromising health and safety?

Align with standard process i.e. annual notifications.

ISSUE 3 – ACCESS BY PATIENTS TO UNAPPROVED MEDICINES UNDER THE SPECIAL ACCESS SCHEME?

Is the Special Access Scheme efficient and effective for Category A patients? Are there issues or concerns with the way in which the Scheme currently runs?

Yes. Eliminate annual reporting requirement and replace with a portal through which a Special Access Scheme (SAS) application can be lodged, include information on products supplied under the scheme and intended unapproved use. Provision of de-identified data could allow the information to be in the public domain for transparency and provide insights into areas of unmet clinical need.

This will eliminate the need for burdensome paper based 6-monthly reporting, and enable TGA to more easily review SAS supply of products.

Mandate standard adverse event and data collection forms on TGA website to support surveillance activities.
Should the Special Access Scheme be revised to narrow the range of circumstances in which TGA approval is required for use of an unregistered medicine in a Category B patient?

If yes, what criteria might be applied to determine when an approval is required?

If no, why not? What do you perceive as the risks of such an approach?

Yes. The same scheme as for Category A patients should be implemented that eliminates the need for prior TGA approval but enables visibility of clinical need for a specific medical condition and/or population over a defined period of time.

ISSUE 4 – INADEQUATE EMPHASIS ON POST-MARKET SURVEILLANCE

Does Australia’s post-market surveillance of medicines need to be enhanced? If so, how might this occur? What would be the features of an effective post-market surveillance system?

If not, why not? Why do you consider the current system effective?

The requirements in Australia align with those of the EU, however the lack of electronic e-health records and inability to easily link existing data sources impacts the ease of managing surveillance activities.

Theme 4: Complex regulatory framework

Is there a role for the TGA in providing a regulatory advice service to product developers/sponsors? If yes, what should the nature and scope of this advice service be? How could risks of regulatory capture be avoided? If not, why not?

There is a role for the TGA to provide regulatory advice. This happens de facto during applications and has resulted in delay for all applications in the approval cycle. This can be alleviated by providing advice outside the assessment cycle.

The nature and extent of advice could be similar to the European Scientific Advisory Groups. Is current guidance material easy to locate, navigate and understand? If not, what are the main issues and concerns? How might this material be improved?

When looking for the regulatory guidance for prescription medicines, current advice is found in:

- Australian Regulatory Guidelines for Prescription Medicines (ARGPM);
- Prescription medicines registration process;
- Mandatory requirements for an effective application;
- General dossier requirements for prescription medicines;
- CTD Module 1: Administrative information and prescribing information for Australia; and
- Specific guidance documents.
Attachment B – Responses to Questions for Consideration

The TGA website could be improved by simplification into:

- Specific Australian requirements (if any are to remain);
- Australian regulatory procedure;
- Australian regulatory requirements (which should directly reference EU requirements as is the case in the ARGPM); and
- A document similar to FDA’s, “FDA Basics for Industry” or EMA’s, “Procedural Advice” would be beneficial.

Is the TGA website easy to navigate? If not, how might it be improved?
Improvements have been made on the TGA website over the past several years. In terms of prescription medicines, the website is not intuitive to lead those who are least knowledgeable through the process for prescription medicines. Consultation with the stakeholders would deliver a more user-friendly website and allowing faster browsing access.

Theme 5: Overly burdensome processes

What TGA processes do you consider most burdensome and why? How might these be improved?

Paper-based and manual systems
The current lack of effective IT infrastructure is a significant barrier to efficient working practices and contributes to delays in information transfer between sponsors and the TGA. The adoption of appropriate technology solutions to support e-submissions (eCTD) will enhance efficiency and resource utilisation for both industry and the agency.

Requirements for paper copies for all submissions should be removed as soon as possible.

Prescription Medicines Registration Process (PMRP)
The PMRP, formerly the Streamlined Submission Process (SSP) has been a great disappointment and lost opportunity for a faster, more transparent and consistent registration process. Increased inflexibility due to rigid operation of the process, loss of opportunities for dialogue and no decrease in times to approval with predicted milestones often not met were not expected outcomes of the redesigned process.

The TGA experiences limitations which results in build-up of cumbersome and duplicative processes to try to compensate, rather than addressing the limitation itself.

Variations
Changes to the ability for Sponsors to self-assess minor variations based on the need for prior approval has increased the regulatory burden for Sponsors:

- The evaluation procedure for variations should be adapted to the level of risk of the change. The ability to ‘notify’ changes should be re-instated; including introducing the EU processes of ‘tell and wait’ and ‘tell, wait and do’.
- Automatic acceptance of decision of trusted regulator for safety-related changes and changes to mature products would reduce burden without increasing risks to public health.
- A one size fits all approach to all clinical changes is overly burdensome and timelines are unreflective of activities performed for minor updates.

Requirements for paper copies for all submissions: while there is wide support for the planned transition to eCTD and this should remove requirement for accompanying paper
copies of submissions, there will be products which have a delayed transition to eCTD (for example, existing registrations), and the requirement for paper copies for variations to these products should be removed as soon as possible.

The requirements for the PI to be included as a package insert in injectables: this is a big burden for industry, particularly concerning provision of updating leaflets in a timely fashion, and also commonly leads to product write off. As healthcare providers have shifted to electronic means for accessing up to date information, there seems no reason to have a requirement for a printed package insert. The TGA website should to be maintained for currency.

GMP certification involves either duplication of overseas assessments or TGA Audit reports. Both are time consuming processes as well as duplicative.

Certified Product Details, with the same information that has been assessed and approved, is provided to another section of the TGA. The testing laboratories can instead be directed to the dossier and this should also become easier as the TGA moves to eCTD.

**Do current regulatory requirements, costs, and timeframes act as a disincentive to the registration of additional indications for medicines?**

No. For medicines under patent protection, the cost to access the market is the cost of doing business (bringing medicines to patients).

**If yes, how might the regulatory framework or processes be changed to reduce the disincentives and/or provide incentives for the registration of additional indications, especially in paediatric populations?**

Extended periods of data exclusivity and options for market exclusivity would provide additional incentives for Sponsors to add indications during the product lifecycle and post patent expiry. For example, in the European Union multiple incentives are available to encourage innovation:

- **Additional indication**: 1 year market exclusivity for new drugs
  1 year data exclusivity for well-established drugs

- **Orphan drugs**: 10 year market exclusivity + 2 years for paediatric indication

- **Rx switch**: 1 year market exclusivity

- **Paediatric indications**: 6 months supplementary patent extension

Simplified registration procedures for drugs with well established ‘off label’ use in clinical practice could be implemented. This could include a system based on review of approved labels and post marketing safety data for drugs registered in other major jurisdictions for at least 10 years for clinical indications not submitted in Australia. This would enable a ‘catch up’ to ensure the most appropriate clinical information is available to physicians.
CHAPTER FIVE: REGULATION OF BIOSIMILARS

Biosimilars

Should the TGA approve the registration of a biosimilar on the ARTG on the basis that:

- a trusted overseas regulator has assessed it as being biosimilar to a reference product available in the overseas market; and
- the sponsor provides evidence that the overseas reference product and the Australian reference product are identical? If not, why not?

Initially at least, there will need to be some local assessment. As discussed in the response to Chapter 4, Theme 1, the greatest value of independent assessment of data by the TGA is to determine the place of the assessed medicine in Australia's clinical context. Biosimilarity is determined based upon the biotechnical data set and results of a limited set of clinical trials. The biopharmaceutical data need to be considered in the light of global supply chain requirements. The clinical data set needs to be reflective of indications approved for the reference product in Australia.

Assessment of biosimilars can also be the subject of work sharing arrangements by the TGA. Whether or not biosimilars will be approved on the basis of a trusted overseas regulator's assessment, the capacity of the TGA to independently assess a dossier if the Sponsor chooses should not be lost.

The requirement that the reference product be sourced in Australia should not be mandatory if the company can show that the overseas-sourced reference product is the same.

What value do you believe an assessment of biosimilarity by the TGA would add in such circumstances?

1. Confirmation of applicability of the biosimilar to the Australian clinical setting.
2. Supply chain considerations such as temperature excursion allowances.
3. Review of the proposed indications for the biosimilar product in comparison to the approved indications of the reference product in Australia.
CHAPTER SIX: OTC MEDICINES
Medicines Australia provides a response in relation to those aspects of scheduling and rescheduling relevant to Prescription medicines, in particular Prescription to OTC switch.

Do Australian decisions regarding the scheduling and/or rescheduling of medicines appropriately balance risk and benefit? If not, why not?

For prescription medicines, the majority of which are Schedule 4, the decision process from a Sponsor perspective is essentially automatic, based on the Delegates referral of new substances under evaluation to the ACMS. However the need for the Delegate to undertake this process is red tape that is an inefficient use of time and resource and should be eliminated. Instead scheduling should be an integrated part of the evaluation process under the responsibility of the TGA.

The current process for rescheduling is complex, not transparent and when compared to other jurisdictions inefficient, risk averse and lengthy. As a consequence Australia lags behind other jurisdictions such as UK, New Zealand, USA and Canada for the number of medicines available for over the counter use. A re-assessment of the process is needed to encourage innovation in the prescription to OTC switch arena. This will help to alleviate the burden on healthcare resources from conditions that are easily self-managed.

Are the current scheduling classifications and factors suitable for appropriately assessing substances based on risk? If not, in what way could they be improved?

The current classifications are appropriate to ensure the appropriate level of healthcare professional oversight is available across the range of supply channels ie direct medical supervision to self-selection in a grocery.

What would be the advantages/disadvantages of adopting a formal methodology for assessment of risks and benefits to inform scheduling decisions? What might such a methodology look like?

The scheduling process should adopt a consistent and transparent methodology that recognises improved access to effective medicines that allows consumers to have more involvement in managing their health and leads to improved clinical outcomes is part of the benefit assessment. The framework adopted by Brass et al (Clin Pharmacol Ther 2011; 90:791-803) has been adopted by other regulators for considering rescheduling applications.

How could the transparency of the scheduling process be improved?

Integration the scheduling process into the evaluation process will support increased transparency and clarity of the process steps.

Are scheduling and registration processes poorly aligned? If so, what approach could be adopted to achieve better harmonisation?

Yes. Integration of medicines scheduling and registration processes, including labelling updates, is required for efficient, timely and transparent decision making.

- The Therapeutic Goods Administration as the medicines regulator has the necessary expertise to undertake a risk-based decision on scheduling with referral to an Advisory Committee only if specific issues need to be addressed.
- In the case of rescheduling medicines from prescription to OTC, the TGA already has an in depth knowledge of the active substance and its post-approval safety profile that is pertinent to a benefit/risk assessment.
• Integration of registration and scheduling on a per product rather than substance basis will encourage innovation in the prescription switch space aligned with the increasing support for consumers to be more actively involved in ‘self-care’ and avoid GPs dealing with readily treatable minor ailments.

• The same concepts for ‘work sharing’ for prescription medicines should apply to rescheduling applications with overseas decisions from comparable regulators and post marketing experience more readily accepted as part of a justification to support a similar schedule in Australia.
  o Exceptions should only occur where there is a significant divergence of local clinical practice that warrants a different approach.

Would efficiency be improved and complexity reduced by introducing parallel processing of scheduling and registration application? And rescheduling applications and related labelling alterations? What are the advantages/disadvantages of such an approach?

Yes. Same comments as noted above apply.
CHAPTER SEVEN: MEDICAL DEVICES

Is the current regulatory framework and classification system flexible enough to accommodate new and emerging medical device technologies? If not, why not? How could it be improved?

The current framework is not deemed sufficiently flexible to be able to cope with the rapidly evolving developments in medical technologies, an issue faced by regulators globally.

In particular software applications or diagnostic tools (IVD’s) designed for use with medicines to serve as effective risk mitigation tools are not easily integrated into a single combined assessment creating significant additional regulatory burden and red tape that can delay access for patients. This is of particular concern in the era of increasing personalised medicine where appropriate patient selection can ensure optimum clinical outcomes. Delays in patient access are further compounded by the divergent reimbursement pathways. An integrated regulatory and reimbursement framework for co-dependent technologies is needed to support early adoption of health innovations that are in the best interests of public health.
CHAPTER EIGHT: FRAMEWORK FOR ADVERTISING THERAPEUTIC GOODS

Should Australia allow advertising of prescription medicines to the general public? If not, why not? If yes, what risks might this create and how could these be mitigated?

Medicines Australia does not support direct-to-consumer advertising of prescription medicines. There is a risk of a potential ‘backlash’ against industry in Australia if communication about prescription medicines is considered to have a primarily commercial intent, which may not be consistent with Quality Use of Medicines (QUM).

However, considerable medicines information from a wide range of sources is already available to the public via internet and other media. In many other industries the ‘Sponsor’ is responsible for directly informing the end user about their products. In an era of increased patient empowerment for managing their health and the wide availability of information on the internet and other electronic media, the ability for Sponsors to directly communicate non-promotional medicines information to the general public ensures the availability of current, accurate and appropriate information to support QUM.

Provision of educational (not promotional) material should be guided by the following principles and supported by industry self-regulatory codes of conduct:

- Restriction of activities to those which provide patient education e.g. CMI awareness; disease information resources to supplement information from health care professionals; availability of patient support programs etc.

- Education to inform the general public and health care professionals (HCPs) of the agreed scope of industry communications relating to education and quality use of medicines.

- Pilot schemes to evaluate responses from patients and HCPs on whether the information provided contributed to improved understanding of medicine use and QUM.

- Potential use of a recognisable ‘logo’ that confirms that information available on the internet or other media is ‘approved’ by the Sponsor and is consistent with industry codes of conduct and therapeutic goods legislation requirements.

Is the current self-regulatory scheme for advertising of medical devices effective? If not, why not? Please provide examples of where the system has failed.

Innovation in the health applications and medical technologies area means guidance supporting self-regulation needs to keep up to date with developments to ensure it is fit for purpose. However, self-regulation is supported as the most appropriate scheme to regulate advertising medical devices whilst protecting public health.

Medicines Australia notes that the recommendations from the 2011 Working Group on the Promotion of Therapeutic Products have not yet been fully implemented. These recommendations, in part, were intended to promote a level playing field between all sponsors supplying therapeutic products, including sponsors of medical devices, in Australia. In particular, it is important that all sponsors of medical devices are covered by the advertising self-regulatory scheme; not just those sponsors that choose to be a member of an industry association that administers a self-regulatory Code of Practice. The lack of Government support for the Working Group’s recommendations that would achieve self-regulation of all Sponsors of therapeutic products means there are still gaps in the effective regulation of advertising medical devices.