AusBiotech submission regarding Review of Medicines and Medical Devices Regulation

To: Review of Medicines and Medical Devices Regulation Secretariat
Department of Health
MDP 67
GPO Box 9848
CANBERRA ACT 2601
medicines.review@health.gov.au

5 January 2015

From: AusBiotech Ltd
ABN 87 006 509 726
Level 4, 627 Chapel St
South Yarra VIC 3141
Telephone: +61 3 9828 1400
Website: www.ausbiotech.org

INTRODUCTION

AusBiotech is pleased to submit to this consultation regarding the Australian regulation of medicines and medical devices, based on comments and submissions from AusBiotech members and from many years of working to grow Australia's strength in biotechnology.

The importance of this review for the highly-regulated life sciences industry should not be underestimated in its ability to deliver real efficiencies, better processes and more appropriate regulation of therapeutic goods, in turn delivering better outcomes for patients.

AusBiotech warmly welcomed the Federal Government's *Industry Innovation and Competitiveness Agenda (IICA)* announcement that Australian manufacturers will be able to register routine (low risk) medical devices and IVDs using certification from European bodies. In real terms, the time taken to register a product is much more important than cost. Decisions that reduce the duplication of processes or reduce the complexity of approval are valued by industry because they cut down the time required to bring products to market. Industry is delighted to see this first step towards adoption of "the principle that if a system, service or product has been approved under a trusted international standard or risk assessment, Australian regulators should not impose any additional requirements unless it can be demonstrated that there is good reason to do so." More broadly, AusBiotech supports the Government's review of regulatory standards and risk assessment processes against this principle.

AusBiotech is a well-connected network of over 3,000 members in the life sciences industry, which includes bio-therapeutics, medical technology (devices and diagnostics), food technology, industrial and agricultural biotechnology sectors. The industry consists of an estimated 900 biotechnology companies (400 therapeutics and diagnostics and 500 – 900 medical technology companies) and employs in excess of 45,000 Australians.

AusBiotech's comments below relate specifically to chapters 4 (on the regulation of prescription medicines) and 6 (on regulation of medical devices).

General comment related to both areas addressed by this submission (prescription medicines and medical devices)

Support work of TGA

AusBiotech would like to commend the work of the Australian TGA and its efforts, under the leadership of Prof John Skerritt, to work with industry to reform and improve its service. It is fundamentally a world-class organisation and is to be congratulated for its achievements in recent times, where it has been seeking and enacting continuous improvement via consultation with stakeholders, with a collegiate attitude.

As a basic principle AusBiotech contends that the TGA should retain its role as sovereign decision-maker and the final arbiter of which therapeutic goods are listed on the ARTG. The TGA should retain the right to refuse listing of a product or to withdraw a listing in the event that post-market

data about a product causes the TGA to find the action warranted. TGA actions should be commensurate with risk and should be aligned with the concepts relating to reducing duplication of effort.

Cost recovery model

The Regulator, operating under a 100% cost recovery model, is not well resourced to conduct its numerous industry-related and non-industry related activities and is out of step with comparable international regulatory bodies. AusBiotech would like to see greater appropriation of public funding to support the TGA's community good activities. Under the current funding arrangements the (private) industry is fully funding both the private and the public activities of the TGA, despite the important public benefit of the role the regulator plays in managing risk to the community.

AusBiotech commends the role that the TGA has played in delivering consumer-good activities to date, however it believes that more should be done. In particular, AusBiotech would like to see the appropriation of public funds to support the TGA provision of training and education services and the development of products to foster innovation in the sector.

AusBiotech is on the record as expressing concern regarding industry subsidy of legitimate TGA activities that are not directly related to the primary remit of industry regulation. Examples of this include necessary government processes and community good activities – required by regulation but diverting resources from the business of regulation. This split of duties is well recognised in other first world countries where a portion of financial support of the regulator comes from government appropriations.

The US, for example, uses a 50/50 model, where 50% of its income is provided by government and 50% is recovered from industry via service users. In the EU 17% of the EMA budget comes from the European Commission and in New Zealand 25% of the regulators funding is derived from government. In these regions the funding model recognises the benefit to industry and the benefit provided to the public. No such recognition exists in the Australian funding model.

Recognition of SMEs

Larger companies and multinationals often have in-house regulatory expertise or can better afford consultant advice, but smaller companies, especially start-ups, are often confounded by the complexity of the system and ill equipped to seek specialist advice.

In a number of other countries, including the US, the regulator assigns funds to provide guidance and education for SMEs, to assist in a better understanding of the regulatory system and how it works. The TGA is to be commended for its training activities, which are actively supported by industry, however these events tend to be oversubscribed and only partly address the needs of the sector.

A better educated SME sector would be a nation building activity for Australia. A program that helps educate young companies would be well received, support the industry's growth, support faster approval of medicines and medical devices and avoid unnecessary re-work.

Within the system, SMEs are at a disadvantage. Apart from their lower internal capability and experience, the cost of registering a therapeutic product is the same for a multinational and an SME. A program that enables early meetings with the regulator is another activity that would substantially assist the start-up end of the industry spectrum and be of broader benefit to Australia's efforts to nurture innovation. This change would also increase the effectiveness and efficiency of the regulator.

Mutual recognition

Australia has the option to recognise approvals from 'trusted overseas regulators'. AusBiotech believes that the TGA should be the sovereign decision-maker and final arbiter of which therapeutic goods are listed on the ARTG, however, the industry supports a mutual recognition model. Therefore rather than full mutual recognition, AusBiotech suggests Australia works with the world's leading regulators – such as the MHRA and FDA – to share data and information to improve efficiencies and safety.

Where products have been approved by trusted overseas notified bodies, the TGA should only provide a review of relevant assessment reports to satisfy itself that the findings are applicable to an Australian context.

AusBiotech recognises that in early stages of confidence building the scope of the scheme is likely to be limited to lower risk products and a small number of trusted bodies. As international harmonisation progresses, AusBiotech would hope to see the TGA maintain a concerted effort to extend the number of notified bodies and product classes involved.

In time it is hoped that trusted notified bodies could include suitably capable Australian organisations.

Reimbursement (PBAC/MSAC)

While these reimbursement avenues are out of scope of this review, it should be noted that they are also embedded in the process of bringing a product to market. Whilst AusBiotech welcomes the efficiency measures that the TGA has put in place in recent times and the work it is undertaking to implement further efficiency measures, AusBiotech would not like to see these measure undermined by inefficient PBAC/MSAC processes. AusBiotech urges the government to review the PBAC/MSAC processes in parallel to the current review.

Programs working well

There are programs within the regulatory system that are working very well and that industry would like to see preserved and kept in-tact.

- CTN/CTX scheme

  For over two decades, Australia's Clinical Trial Notification (CTN) and Clinical Trial Exemption (CTX) system has been a global benchmark for best practice in reducing the regulatory

burden on clinical trial sponsors. In fact, it is one of the few clear advantages Australia has in attracting global investment in clinical trials and thereby providing early patient access to new treatments.

An overwhelming majority of commercially sponsored clinical trials conducted in Australia are performed under the CTN/CTX system.

The system as it is eliminates unnecessary duplication and saves clinical trial sponsors in Australia a significant amount of time and money. Savings from these measures are used to other research projects, which in turn enhances the competitiveness of Australia as a destination for clinical trials.

- R&D Tax Incentive

The Research and Development (R&D) Tax Incentive has been welcomed as the most important public policy positively impacting the sector. The policy intention was about encouraging research and development and its spillover benefits for the community.

Any change that might undermine the program would effectively wind back years of work and would jeopardise the momentum of spillover benefits, including the increase in clinical trial activity and regulatory approvals sought.

Given there is so little incentive for innovation remaining in Australia, AusBiotech and others have been advocating for end-to-end tax reform to open the pipeline from early research through to regulatory approval and commercialisation.

Benchmarking against US and EU

Given the global nature of regulated therapeutic goods, and the need companies have to make strategic decisions about where and when to register products, benchmarking the TGA's performance against the US and EU and releasing such information to the public would be a helpful step. Noting the comparison of median days to achieve registration in the discussion paper, it is assumed that this information is already collected for internal use and reporting purposes. Releasing the information would assist industry in its decision making processes and provide appropriate transparency of the TGA's performance.

REGULATION OF PRESCRIPTION MEDICINES

General comments

AusBiotech supports the following general principles in relation to the regulation of medicines.

1. The TGA should retain its role as the first line regulator of medicines in Australia. TGA must retain its status as sovereign decision-maker and the final arbiter of which products are listed on the ARTG.
2. The TGA should retain the right to delist a product in the event that post-market data about a medicine causes the TGA to find the action warranted.
3. Duplication of regulatory processes should be avoided and where possible the TGA should develop trusted relationships with other regulators to minimise duplication.
4. Without compromising consumer safety the TGA should prioritise the timeliness to approve a product over the administrative cost. AusBiotech supports fast track processing with a similar priority review process to the FDA.
5. Accelerated access to higher risk products should be assessed using a risk-based approach.
6. The TGA is responsible for providing clear guidance to industry regarding the Australian regulatory framework for medicines and should provide clear guidance about timelines for the regulatory pathways within the TGA's regulatory framework.

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'?

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

AusBiotech support the use of International Conference on Harmonisation (ICH) categorisation to identify broadly acknowledged 'tier one' regulators i.e. European Medicines Agency, US Food and Drug Administration, Japanese PMDA.

The extension of trusted regulators to other international regulators should be treated by the TGA as the extension of the principles of regulatory harmonisation. In time it is hoped that trusted notified bodies will include suitably capable Australian organisations.

Medicines that have been approved for the same indications by a trusted overseas regulator should be approved for registration on the ARTG only after a formal review of the trusted overseas regulator's evaluation report to confirm the medicines applicability in the Australian clinical setting. The TGA must retain its status of sovereign decision-maker and final arbiter of which medicines are listed on the ARTG.

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?

On a case-by-case basis, where there is a known difference in assessment between two trusted regulators, the TGA should review the reasons for rejection in its own review process. If the grounds for rejection apply to the Australian clinical setting then the TGA may wish to refuse to list the medicine on the ARTG.

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

Where the TGA becomes aware of post-market data that would cause the TGA to have concern about the health and safety of Australian consumers then the TGA should review the status of the medicine in concern. The TGA should retain the right to delist a product at any time should it feel that the action is warranted.

Issue 2 – What does approval of a 'product' mean?

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?

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?

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?

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

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

Where a product has been approved for the same indications by a trusted overseas regulator then the TGA should list the medicine on the ARTG only after reviewing the assessment report and satisfying itself of its applicability to the Australian clinical setting.

In the event that an overseas assessment for a medicine to be listed on the ARTG is found to be unsatisfactory, the TGA should retain the authority to demand a re-assessment. It should aim to keep this assessment to a minimum – a full assessment required only under defined circumstances.

Issue 3 – Is there good reason for Australia to impose additional requirements?

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

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

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?

The TGA as the sovereign decision-maker and final arbiter of which products are listed on the ARTG should retain the capacity to impose its own conditions upon any product being listed on the ARTG. Additional conditions imposed by overseas regulators should form part of the TGA assessment of a medicine before it is listed on the ARTG.

The TGA should make every effort to minimise additional constraints as these will inevitably lead to delays and regulatory burden both during the application period and during the post-market assessments.

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?

AusBiotech highly recommends the introduction of an accelerated approval program. Not only would this provide the opportunity for therapeutic products to reach patients sooner, especially in areas of unmet need and for serious and life threatening illness, but would offer (currently unavailable) options for industry. The program/s success would be determined by the ability to provide certain timeframes for assessment and this should be a key feature of any design chosen.

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?

AusBiotech supports a flexible approach to the accelerated approval without introducing an overly complex framework. A system broadly modelled on the US approach that allows for multiple paths should be considered. Clear and publically available guidance should support the TGA's framework for the review of medicines to ensure advice and guidance provided by TGA staff is clear and unambiguous and the industry is fully informed about the options available.

AusBiotech strongly urges the TGA to offer a priority review pathway for breakthrough medicines that target serious or life-threatening conditions. A scheme similar to the FDA Breakthrough Therapy Designation should be considered by the TGA. The TGA should be arbiter for whether such approvals take precedence over other accelerated and regular approval processes.

An accelerated pathway that offers industry the opportunity to pay a higher premium for faster approval processing should be considered. Such a pathway requires dedicated TGA resources and should not have a negative impact on other TGA processes and will not if funded by the sponsors.

Whilst biosimilars are the subject of Chapter 5, the concepts above are equally applicable to these medicines in that they are scientifically innovative and can offer significant savings to the public healthcare.

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

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?

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

The TGA should, by law, have the mandate to add or remove products from the ARTG. Any decision to withdraw a medicine from the ARTG should be supported by a publically-available justification for its removal. For clarity, unsuccessful applications for ARTG listing should not be made publically available due to the risk of misinterpretation about the underlying reasons for the nature of the refusal.

Theme 3 - Regulatory requirements are not commensurate with risk

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?*

AusBiotech is supportive of the TGA adopting a risk-based regime where the application fee and processing time is related to the overall level of risk to users. For variations to low-risk medicines, or for low-risk variations to moderate-risk products, there should be a corresponding lower application fee and shorter timeline for approval.

The TGA should develop clear guidance on the definitions of what constitutes 'low risk variations' and should retain the role of final arbiter of risk classification.

The TGA should provide clear statements of the costs and time expectations for approval of variations for the different risk categories.

Similarly, generic medicines are also low-risk compared to the respective proprietary medicines. It is appropriate that the current pathway for registration of new generis, as well as the process for variations, is evaluated in this context.

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?

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?

Is the TGA website easy to navigate? If not, how might it be improved?

The TGA has an important role in providing regulatory advice to industry. In particular the TGA should be responsible for providing better and earlier regulatory advice to SME and start-up organisations as these organisations are critical to the Australian health system but are often unable to pay for expert advice or are unaware that they need expert advice.

Most AusBiotech members report that the current TGA website is relatively easy to navigate and that materials are easily located. However, members have also commented that the resources available on the TGA website are sometimes inadequate, inconsistent or that appropriate guidance is not available. Finally they report that officials within the TGA can at times offer ambiguous, incomplete or conflicting advice.

AusBiotech strongly urges the TGA to consider reviewing its regulatory advice services and to consider the development of programs to support industry particularly focussing on the needs of SME organisations.

As a minimum the TGA should review its regulatory advice services and where necessary strengthen or develop:

- Clearly written guidance materials to support the TGA regulatory framework and regulatory processes;
- A schedule of costs and timelines for regulatory pathways within the TGA regulatory framework;
- Support programs to assist SME organisations.

TGA should be allocated an appropriation of public funds to support the development of programs that support start-up, and small businesses into the industry. The TGA is encouraged to consider programs such as those run by the FDA that support entrepreneurs and innovators by providing early and clear information about Australia's regulatory framework.

Theme 5 - Overly burdensome processes

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

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

- *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?*

Current TGA processes are not considered by AusBiotech to be overly burdensome.

AusBiotech has suggested several ways the regulatory framework could be enhanced through harmonisation, fast track processing and the provision of stronger guidance documentation and advice services.

In addition, some consideration could be given to electronic submissions without the requirement for paper-based documentation.

REGULATION OF MEDICAL DEVICES

General comments

AusBiotech has observed that at times medical devices are held to standards of evidence used for medicines – this is inappropriate. For devices:

- Much greater emphasis of risk assessment should be on the assessment of post-market data.
- Pre-market assessment should be streamlined as much as possible utilising information from international regulators or, in the case of co-dependent or hybrid devices, from data relating to the risk associated with the different device components.
- The TGA should consider a pragmatic risk-based approach to changes to a product. Clear guidance should be developed to define what constitutes 'low risk changes' that could then be exempt from re-assessment.

AusBiotech and its member medtech and IVD organisations applaud the TGA review of how assessment reports from overseas regulator could be used to streamline TGA approvals of products for listing on the ARTG. AusBiotech believes that efficiency gains from greater harmonisation of Australian premarket assessments with other regulatory agencies will allow the TGA to redirect resources toward the more valuable post-market data capture and assessment.

The quantity and quality of post-market data is growing rapidly and offers the TGA and industry several valuable ways to improve the risk management of devices; through improved surveillance, improved targeting of product development, and through faster release of risk-mitigated products. The shift of emphasis from pre-market assessment to post-market surveillance and assessment is one of the biggest areas of opportunity for TGA if the burden of pre-market assessment can be reduced. Post market analysis needs to be more comprehensive and not focus exclusively on adverse events.

Theme 1 - Duplication of regulatory processes

Issue 1 – How might a trusted overseas regulator be defined?

Should the TGA undertake its own assessment of the competency of EU notified bodies? If yes, how might this occur?

- *If not, why not? Alternatively, given the concerns with the EU system, should Australia look to recognise other international regulators as 'trusted' for the purpose of device approvals?*
- *If yes, what criteria should apply in determining whether or not an overseas regulator is trusted?*

The TGA should satisfy itself that the EU notified bodies it recognises are competent in a manner that is most resource efficient for the administration. TGA should extend its practice of approving inclusion of devices on the ARTG base on approval by trusted overseas regulators.

Criteria of assessment could be to include Global Harmonization Task Force (GHTF) countries that use summary technical documentation and have in place mutually recognised international standards in a similar fashion to the Canadian Medical Devices Conformity Assessment System audit

criteria. In this way customers of the TGA could refer to the list of trusted bodies that are approved by the TGA.

AusBiotech members believe that through harmonisation of Australian pre-market assessment processes with other regulatory frameworks, premarket assessments can be undertaken more efficiently allowing TGA resources to be redirected towards post-market surveillance.

The extension of trusted regulators to other international regulators should be treated by the TGA as the extension of the principles of regulatory harmonisation.

Issue 2 – Is there a good reason for Australia to impose additional requirements?

Should the TGA approve the inclusion of a medical device on the ARTG on the basis that it has been approved for the same purpose by a 'trusted' overseas regulator?

- *If yes: should this occur regardless of the class of the device?*
- *How could concerns about the quality of some overseas conformity assessments be managed?*

The view of AusBiotech members – including manufactures of all classes of devices – is that it is logical and desirable to extend the designated trust to regulators for all classes of device. However, AusBiotech recognises that this is likely to be difficult to implement and suggests a staged process. In the short term, during the transition phase, trust could be extended to international regulators of GHTF countries for Class I, IIa, and IIb devices and that Class III devices would follow at a later date. As the program designed to assess suitable foreign regulators is established the TGA can expand to other members of the International Medical Device Regulators Forum in the future as harmonisation progresses.

When the TGA considers extending trust to include regulation of Class III devices it may want to consider further staging of implementation, for example Class III devices (or similar) that have undergone PMA review in the USA, or Shonin review in Japan, may be considered as having undergone sufficient review for registration in Australia.

Greater emphasis should be put into managing the quality of overseas conformity assessments through post-market surveillance of products.

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

Safety, quality or efficacy should be considered as common considerations and standardised as much as possible between participating regulators. TGA should retain the flexibility to include additional requirements that may be specific to the Australian context.

Where there are differences in device classification between Australia and the EU, should sponsors be required to meet additional conformity assessment requirements? If not, why not?

Should Australia adopt the EU classification system? If not, why not? What are the strengths of the Australian device classification system that cannot be found in the EU system?

Medical device and IVD classifications should be harmonised as much as possible. Australia should actively engage with global regulatory harmonisation activity to ensure where possible that classifications are based on agreed standards and levels of evidence. The TGA should endeavour to ensure that:

- Australian classification of devices and IVD products are based on the most recent global trends in harmonisation. In some cases these may be superior to the EU regulations as is currently the case with IVD regulations.
- Where there are differences in classification systems, there needs to be clear guidelines for TGA staff and industry on how to bridge the gap in assessment requirements. The TGA should actively work to minimised the incidence of differences between Australian classifications and generally agreed device classification. Where Australian classification results in higher levels of assessment required then the TGA should provide guidance to, and help facilitate, manufacturers seek an appropriate level of assessment through their notified body.

Should Australia maintain Australian specific requirements with respect to labelling and post market monitoring? If not, why not? If yes, what value do these requirements add?

Post-market surveillance is an important area for consideration and has been addressed in Theme 3, Issue 3. AusBiotech recommends that the TGA should place greater emphasis on post-market surveillance. Ideally the specific requirements for post-market monitoring of devices and IVD products should be part of the global harmonisation of device and IVD product regulation.

Issue 3 – What is meant by product approval?

Should a difference in a medical device that has been approved by a trusted overseas regulator necessitate a further assessment by the TGA in circumstances where that difference may impact safety, quality or performance? If not, why not?

- *If yes, should the assessment by the TGA be limited only to those aspects of the application that are impacted by the difference?*
- *Would this approach apply to all classes of medical devices?*

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

- *Would this approach apply to all classes of medical devices?*

As a general principle, trusted overseas regulators should be considered equivalent to the TGA for assessing the class, safety, quality and performance of a medical device or IVD product.

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

Currently, marketing provisions are governed under consumer production laws and should not be considered by the TGA.

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?

The TGA should, as a basic principle, maintain the capacity to impose its own conditions. There should be an onus of responsibility on the TGA to justify to the Australian public why these conditions should differ from generally accepted globally harmonized conditions.

Theme 2 - Lack of flexibility

Issue 1– Accelerated access

Should Australia introduce an accelerated approval program(s) for higher risk medical devices? If yes:

What eligibility criteria should apply to the accelerated approval pathway? That is, under what circumstances could a sponsor apply for accelerated approval of a device?

What are the potential risks and benefits of such programs and how might the risks be managed and the benefits maximised?

If higher risk medical devices 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 clinicians and/or consumers to the provisional approval and its implications?

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

At present, manufacturers (both locally and overseas) of some Active Implantable and Class III medical devices must go through a Level 2 audit. Level 2 audits are notionally performed within 60 TGA days. However, this is currently met for only 57% of applications (TGA data). The protracted time for Level 2 audit causes a significant delay in the launch of these products to the Australian Market. In furthering the confidence-building exercise, AusBiotech suggests TGA consider options for expedited processing of applications currently subject to Level 2 audit where the devices are CE certified by a notified body where TGA has established confidence. Options could include:

- Option 1: Waiver of Level 2 audit with selected post-market audits following ARTG inclusion.
- Option 2: Abbreviated audit where the manufacturer/sponsor is able to supply a recent satisfactory Notified Body audit report and only the Notified Body report is reviewed by TGA.

Long term, AusBiotech believes that the benefits to society of introducing an accelerated approval program for medical devices outweighs the risks associated with doing so. Risks associated with individual patients could be managed in the same way as are done under the current scheme for medicines or a system similar to the USA's accelerated approval pathway.

What additional post-market surveillance would need to be in place for medical devices that were provisionally approved?

A post-market surveillance system (discussed in Theme 3, Issue 3) would be an important resource for mitigating the risk associated with the introduction of an accelerated approval program.

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 general consensus amongst AusBiotech members is that the current regulatory framework and classification system is not flexible enough to accommodate new and emerging medical device technologies. Members highlighted that:

- TGA processes are too slow and costly;
- The lack of guidance documentation regarding how to address the risks of new technologies or how to bring novel new devices to market is causing delays and substantial costs to sponsors of these products. Guidance documentation would allow consistency of message from TGA, would assist TGA staff to support sponsors and would support sponsors – particularly SME organisations – to understand and comply with the system. Advances in

hardware, software and telecommunications were given as examples of where there is confusion about what constitutes a device and where documented guidance could reduce the confusion without costly delays; and

- The most important factor for industry is reliability and consistency.

Theme 3 - Regulatory requirements are not commensurate with risk

Issue 1– The balance between risk management and regulatory burden

Does the current regulatory framework for medical devices in Australia provide an appropriate balance between managing risk and minimising unnecessary regulatory burden? If not, why not? Please provide examples.

Should low risk medical devices that are not subject to an independent conformity assessment be included on the ARTG?

- *If not, why not? Are there any risks involved in not including such products on the ARTG?*
- *If yes, why? What are the benefits of these products being included on the ARTG?*

In general AusBiotech members reported that the current regulatory framework was commensurate with the level of risk of the device. Members expressed frustration at time delays that have been caused by discrepancies between conformity assessments by different regulators.

AusBiotech believes that all therapeutic goods sold in Australia should be included on the ARTG. The ARTG is an essential management tool of medical products that are approved for sale in Australia and it is also used by other markets as evidence of TGA approval in Australia.

Issue 2– Variations to medical devices

Should Australia adopt a risk-based regime for variations, which allows notifications and/or annual reporting for changes to medical devices that are at low risk of impacting the quality, safety, or performance of the device?

- *If yes, what might such a regime look like? How might notification/reporting procedures be designed so as to minimise burden on sponsors?*
- *If not, why not?*

AusBiotech believes that a risk-based approach to product variation would be an important step towards minimising regulatory burden. Low risk changes should be allowed without formal review. Guidance on what constitutes 'low risk changes' should to be clearly described in supporting documentation – for TGA staff and industry. The TGA should retain the right to question changes although this should be kept to a minimum. A similar approach to the medicines assessment of risk could be used to develop the scheme.

Issue 3– Post-market surveillance and supportive data collection and analysis

Does Australian have the balance right between pre-market and post-market regulation of medical devices?

- *If not, why not? How could it be improved?*

What are the features of an effective post-market surveillance system?

AusBiotech members believe the TGA does not have the balance of pre-market and post-market regulation right, that greater emphasis and resources should be applied to the post-market assessment of medical devices.

Medical devices differ substantially from medicines with respect to the value of pre-market and post-market risk assessment data. The current regulation of medical devices by the TGA is heavily pre-market with little to no proactive post-market surveillance. This is at odds with the great majority of data that is available to assess the clinical application of medical devices – data that is difficult if not impossible to assess in pre-market assessments due to the individuality of many medical device procedures.

AusBiotech believes that the TGA should investigate changes to the assessment of devices that:

- Reduce the regulatory burden and time taken for approval of medical devices to be listed on the ARTG – particularly for lower risk devices, devices that have already been through an international assessment or for products where risk assessment data is available internationally;
- Captures post-market data from clinicians and consumers for assessment by TGA and product manufacturers;
- Does not diminish the capacity of the TGA to assess medical devices, but that shifts the burden of assessment (and corresponding TGA resources) from the pre-market assessment of devices to a post-market surveillance and assessment system.

AusBiotech members believe that strengthening the post-market surveillance of medical devices will lead to:

- Improved surveillance of the risks associated with medical devices leading to better assessment of the nature of risks associated with products in the marketplace;
- Better alignment of TGA systems with the nature of product development trends. Far more consumer data is becoming available for products in the marketplace – data that is exceptionally valuable for the assessment of risk and benefit and which should be available to TGA risk assessment teams.
- Faster introduction of new technologies into the Australian marketplace. Whilst shifting the emphasis from pre- to post-market assessment may not reduce the overall administration of a regulatory regime for a new product, getting a product to market faster has a major impact on the benefit of a product to businesses (and to consumers).

Issue 4– Access to unapproved medical devices

Has the regulatory framework for IVD's resulted in a reduced emphasis on clinical best practice? If so, how. Please provide examples.

Should there be statutory timeframes for assessment of applications for inclusion of an IVD on the ARTG?

The regulatory framework for IVD's has resulted in reduced access to tests incorporating new clinical techniques. Members report confusion over the regulations regarding the scope of the regulations and how they apply to products.

AusBiotech IVD members have reported that the new regulatory pathways are more burdensome for a larger number of devices, and that entry to market is slower than under the previous framework.

Theme 4 - Overly burdensome processes

Issue 1– Multiple systems and manual processes

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

AusBiotech members outlined the most burdensome processes:

- Verification and assessment of products which should be done as a single process. If a device is assessed and granted conformity assessment certification by the TGA, it should automatically be eligible for inclusion in the ARTG. Members reported that after negotiating with the TGA during the conformity assessment process, they had to renegotiate with a different TGA team during the application for inclusion in the ARTG. They found this doubling up of processes to be inconsistent, time consuming, frustrating and a cause of costly delays.
- The manual application for approval of marketing materials was reported to be burdensome and slow. The documentation provided by the TGA should be updated to be in-line with current regulations and use a standardised, risk-based review to minimise the time for approval.

Issue 2– Process for inclusion of medical devices on the ARTG

How might the processes required to include a device family on the ARTG be streamlined without undermining public health and safety?

Are there other concerns with the inclusion of devices on the ARTG? How might these be addressed?

AusBiotech members reported inconsistencies of assessment within device families – such as hip replacement devices – where the application of devices are similar but the products are treated separately. Devices within a family (defined by application) should be reviewed at the same time and by the same review team to avoid duplication and inconsistency of assessment. The TGA should review how devices are categorised so that more consideration is given to the application of the device rather than a device's technical description.

Issue 3– Instructions for medical devices

Should the TGA allow a broader range of permissible formats for instructions for the use of medical devices? If not, why not?

Permissible formats for instruction on the use of therapeutic goods should be consistent with consumer demands and technological change. There are safety, convenience and cost-savings reasons for moving away from paper-based formats to electronic and web-based formats.

Issue 4 – Registration of additional intended purposes for a device

Do current regulatory requirements, costs, and timeframes act as a disincentive to the registration of additional intended purposes for medical devices?

- *If yes, how might the regulatory framework or processes be changed to reduce the disincentives and/or provide incentives for the registration of additional intended purposes?*

AusBiotech members have consistently stated that current regulatory requirements, costs and timeframes are disincentives to the registration of additional intended purposes for medical devices. If a product has been recently assessed (within the past few years), the TGA could waiver the requirement for an additional – duplicative – assessment. It should consider implementing a process that leads to a quicker risk-based assessment of the change in purpose or dosage.

Theme 5 - Complex regulatory framework

Issue 1– Categorisation of medical devices

Is the classification system for medical devices too complex? If yes, how might it be simplified without impacting public health and safety?

Do manufacturers require assistance, such as online decision tools, to assist them to correctly classify medical devices? If not, why not?

- *If yes, what sorts of assistance would be most effective?*

No AusBiotech members described the classification system for medical devices as too complex, however most said that there is poor guidance documentation. Clear, easily accessible guidance documentation and decision tools would support consistency of messaging between TGA staff and would greatly assist businesses to understand the class applicable to a particular product.

Up-to-date guidance documentation (guidelines, case studies etc.) and decision tools (decision trees, wikis etc.) were considered by AusBiotech members to be a high priority for TGA to support businesses. Such tools would be particularly helpful to – but not limited to – SME or start-up medical device organisations that often do not have dedicated regulatory affairs personnel or the resources to fund consultants to categorise the device.

Is the pre-market assessment of medical devices considered overly complex in other ways? If yes, in what way? What are the major pressure points and how might these be addressed?

As discussed previously in Theme 3, the TGA balance of pre-market and post-market regulation is overly weighted to pre-market assessment. In particular, pre-market clinical assessments are overly complex with unwarranted expectations of the level of clinical evidence required by clinical reviewers. A regulatory framework should be developed that supports the categorisation of risk and standards of evidence required.

In addition members have reported that the regulation is overly legalistic and that the TGA should consider mirroring the approach taken by the FDA to draft parts of the federal regulations in 'layman's terms'.

Is there a role for the TGA in providing a regulatory advice service to product developers/manufacturers/sponsors? If not, why not?

- *If yes, what should the nature and scope of this advice service be? How could risks of regulatory capture be avoided?*

A TGA regulatory advice service to product developers/manufacturers/sponsors would be welcomed by AusBiotech members. Members expressed consistent frustration with the lack of formal mechanisms to consult with the TGA prior to the application for assessment. Companies that have

experience with the USA system have suggested that the TGA consider mirroring the FDA example that has non-binding and binding meetings to discuss application requirements.

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?*

Is the TGA website easy to navigate? If not, how might it be improved?

The TGA website, with its recent upgrades, is considered suitable, comprehensive and easy to navigate.

Issue 2– Transparency of regulatory decisions

Should information about regulatory decisions in respect of medical devices be publicly available? For example, an evaluation report or other relevant information.

- *If not, why not? What do you see as the risks?*
- *If yes, how would this benefit consumers, clinicians and industry? How could any risks be managed?*

AusBiotech is cautiously supportive of transparency of regulatory decisions.

AusBiotech believes that the publication of regulatory decisions should be limited to applications for inclusion only and not the publication of conformity assessments. Further, rejected inclusion-application material should not be published since the reasons for rejection can be multi-faceted and the information could be subject to misinterpretation.

AusBiotech members have expressed concern that information released by the administration should be:

- For the public good;
- Factually correct;
- Not commercial-in confidence;
- Unambiguous, and not prone to being misinterpreted.

Should other regulatory findings relating to medical devices be made public, for example, reports on audits or post-market reviews?

- *If not, why not? What do you see as the risks?*
- *If yes, how would this benefit consumers, clinicians and industry? How could any risks be managed?*

Could the regulation of medical devices be made more transparent in other ways? If so how, and what would be the risks and benefits of the proposed approach?

Product recalls (and the reason) should be made public and handled by the TGA.

Other regulatory findings relating to medical devices should not be released as members felt this would increase the risk that clinicians or users would react inappropriately and may unnecessarily undermine confidence in a particular product.

Issue 3– Interaction with other regulatory frameworks

Is the system overly complex for manufacturers/sponsors of devices using hybrid/convergent/ co-dependent technologies? If yes, how could the process be streamlined without undermining public health and safety?

AusBiotech members who manufacture or sponsor hybrid/convergent/co-dependent technologies report that the TGA's regulatory framework is particularly complex and ill defined. Where the separate elements of such devices have been assessed independently for the intended use and other variables are consistent, then there should be a streamlined approval process. Further, alignment between government departments on requirements, process and timelines would be helpful. Where there are overlaps in responsibility, consideration should be given to assigning precedence to one department to avoid duplication of effort.

Given the complexity of this category of products, clear guidance documentation is essential – both to help the departments involved give clear messages to industry, and to support industry to understand the department's regulatory framework. Clear guidance would greatly help to minimise the burden of these regulations.

Issue 4– Consumer understanding of medical devices regulation

Is the regulation of medical devices transparent enough in terms of informing health professionals and consumers about the level of scrutiny that a device has undergone? If not, how could it be improved?

AusBiotech does not believe that greater transparency about the level of scrutiny of a device will have any benefit to public or health professionals' opinion of either the TGA or the product of concern.

Should there be a system for medical devices similar to the AUST R and AUST L system for medicines? If not, why not?

AusBiotech does not believe that an AUST R and AUST L equivalent system for medical devices is required. It would likely to lead to confusion and have little benefit to consumers or practitioners.