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收 106. 06. 26 文
檔號： 106453

發文日期：中華民國106年6月21日
發文字號：FDA器字第1061604689號
速別：最速件
密等及解密條件或保密期限：
附件：澳洲TGA草案文件1份

主旨：有關澳洲藥物管理局(Therapeutic Goods Administration, TGA)預告將考慮採用他國之上市證明一事，詳如說明，請查照。

說明：

一、依據澳洲TGA今（2017）年5月22日公告之草案文件“Comparable overseas regulators – medical devices: Criteria and implementation”（影本如附），該國將考慮採認其他國家之醫療器材上市證明，俾將其用於醫療器材之上市核准；該草案徵求意見至今年6月30日止。

二、為深化台澳雙邊醫材產業交流，增進我國醫材產業出口便利性，請協助將前揭草案資訊轉知所屬相關會員(https://www.tga.gov.au/consultation/consultation-comparable-overseas-regulators-medical-devices)，請其評估是否就該草案內容向TGA提出相關意見，以促成澳洲將我國納為上市證明之採納國家之一。另，亦請提供有銷售醫療器材至澳洲之國內製造業者名單供參。

正本：台灣醫療暨生技器材工業同業公會
副本：

署長 吳秀梅

Australian Government

Department of Health

Therapeutic Goods Administration

Comparable overseas regulators – medical devices

Criteria and implementation

Version 1.0, May 2017

TGA Health Safety Regulation

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All submissions received will be placed on the TGA's Internet site, unless marked confidential. Any confidential material contained within your submission should be provided under a separate cover and clearly marked "IN CONFIDENCE". Reasons for a claim to confidentiality must be included in the space provided on the TGA submission form. For submission made by individuals, all personal details, other than your name, will be removed from your submission before it is published on the TGA's Internet site. In addition, a list of parties making submissions will be published. If you do not wish to be identified with your submission you must specifically request this in the space provided on the submission form.

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Purpose and scope

The Therapeutic Goods Administration (TGA) is seeking comments on the use of marketing approval for a device in an overseas market to support inclusion of the device in the Australian Register of Therapeutic Goods (ARTG). This includes proposed criteria to identify comparable overseas regulators and mechanisms to allow consideration of such overseas marketing approvals when deciding whether a medical device should be approved for the Australian market.

The purpose of the criteria is to identify regulators with similar standards to the TGA, and to allow confidence in the assessment undertaken by the regulator or the third parties that are oversighted by them, so as to avoid duplication of work in Australia without compromising public safety.

We are specifically looking for feedback on criteria for identifying:

- comparable overseas regulators to allow consideration of their market authorisation decisions; and
- overseas designating authorities that are comparable to the TGA to allow confidence in the third parties they designate.

This consultation focusses on how these criteria will be applied within the medical devices context. Submission of your views on this proposal is appreciated.

Background

MMDR

The expert panel conducting the Review of Medicines and Medical Devices Regulation[1] (MMDR) made recommendations aimed at streamlining the TGA's processes for including medical devices in the Australian Register of Therapeutic Goods, in order to improve the timeliness of access by Australian consumers to new medical devices.

The Government has decided[2] that the TGA should make greater use of marketing approvals for devices in overseas markets when the device has been approved by a third party that has been designated by an authority that is similar to the TGA or by a comparable overseas regulator (in line with MMDR Recommendation 15, Pathways 2A & 2B).

The Government accepted-in-principle the MMDR review recommended that the TGA develop and apply transparent criteria for identifying comparable overseas regulators and designating authorities (Recommendation 17), taking into consideration:

A. Population demographics and health outcomes.

B. Adoption of Global Harmonisation Taskforce (GHTF) guidelines.

C. The track record of the organisation in evaluating/assessing medical devices and/or oversighting the evaluation/assessment of medical devices.

D. Independence and impartiality.

1 http://www.health.gov.au/internet/main/publishing.nsf/Content/Expert-Review-of-Medicines-and-Medical-Devices-Regulation

2 Government response to the MMDR Report - https://www.tga.gov.au/sites/default/files/australian-government-response-mmdr-2016.pdf

E. Transparency of systems and processes.

F. Technical competence.

G. Utilisation of Quality Management Systems.

H. Accountability, including independent review/audit.

I. Reporting and communication.

J. Timeliness of access to information and data.

K. Compatibility of evaluation/assessment of medical devices with the Australian Essential Principles.

Consequently, this paper expands on the factors for consideration outlined in the MMDR report in developing the proposed criteria and outlines how these would be applied.

In using international approvals to support Australian Register of Therapeutic Goods (ARTG) inclusion, the TGA would continue to make the final regulatory decisions, ensuring that quality and safety are not compromised and that the Australian context is taken into account. These considerations (outlined in MMDR Recommendation 18) include whether:

A. the device has been correctly classified under the Australian regulatory framework; and

B. the 'marketing approval' documentation is in complete and correct and meets Australian requirements; and

C. the product is identical to the one assessed by the comparable overseas regulator or designated third party, having been made in the same manufacturing facility, of the same materials, and for the same intended purpose; and

D. in meeting the Australian requirements the device complies with the relevant state-of-the-art standards for use in the Australian health system; and

E. there are any specific issues regarding applicability to the Australian context that need to be examined, including in respect to post-market monitoring and risk management; and

F. proposed product labelling and product information/instructions are appropriate and consistent with Australian requirements; and

G. any conditions or provisions that are imposed on the marketing approval of the medical device under the terms of the overseas marketing approval are able to be replicated and complied with in the Australian market.

H. To ensure clarity and consistency in processes, the MMDR review also recommended that the TGA develop and apply transparent criteria for identifying comparable overseas regulators and designating authorities (Recommendation 17). Consequently, this paper expands on the draft criteria outlined in the MMDR recommendations and outlines how these would be applied.

Current use of overseas assessments

TGA may currently use assessments by overseas regulators or the bodies they designate in two key ways:

- ***Conformity assessment:*** may be used to abridge assessment (to a lesser or greater extent) where evidence of assessment by an overseas regulator is submitted as support for the application. This is typically the detailed audit or design examination reports from European notified bodies. The TGA reserves the right to conduct a full assessment if the TGA is not fully satisfied with the evidence of compliance provided by the applicant.

On-site audits of the quality management system assessments may be abridged based on site visits and detailed supporting reports from overseas regulators. It is anticipated that MDSAP reports (discussed later in this paper) may also be relied on for this purpose.

- ***Inclusion in the ARTG:*** As the Australian and the EU regulatory requirements are currently similar[3], TGA legislation permits that certificates issued by European notified bodies[4] may be accepted as the evidence of the application of the appropriate conformity assessment procedures to the devices for the purposes of seeking pre-market approvals for those devices for supply in Australia (with some qualifications[5] and exceptions[6]). In practice European notified bodies' EC certificates support more than 90% of existing ARTG entries[7].

Even where a medical device has been approved by a comparable overseas regulator, Australian approval is not automatic. Differences between Australian and overseas regulatory requirements, difference in the time when the medical device was assessed (potentially there can be significant changes in a device if some time has elapsed between the overseas and Australian assessments), post-market data including records of adverse events, and different expectations regarding safety of medical devices in Australia and overseas may result in rejection of an application for pre-market approval of a medical device even though it has been approved overseas. There may also be some scope differences which preclude use of approvals from recognised comparable overseas regulators, such as where particular devices are classified differently in different jurisdictions (discussed in more detail below).

It is anticipated that similar issues will arise when relying on approvals from other regulators, and these will need to be managed to enable use of approvals from other overseas regulators. Based on lessons learned in relying on European certification, the criteria for the selection of overseas regulators are designed to ensure overseas regulators are comparable, and the differences between regulatory approaches are fully appreciated and managed. Existing application audit arrangements will remain to enable the risks associated with the lack of direct oversight of the regulatory approval to be managed.

International engagement

Global regulatory convergence

The TGA is a founding member and active participant in the International Medical Device Regulators Forum (IMDRF). This group is the successor organisation to the Global Harmonisation Task Force (GHTF), of which the TGA was also a founding member. The GHTF guidance material underpins the medical device regulatory frameworks of many of the IMDRF member nations, including Australia.

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3 The European and Australian regulatory frameworks are both aligned with the GHTF framework, with close parallels between the European 'Essential Requirements' and Australian 'Essential Principles', very similar classification rules, and comparable manufacturers' conformity assessment procedure requirements.

4 EC certificates issued under EU Medical Devices Directive 93/42/EEC (MDD), EU Active Implantable Medical Devices Directive 90/385/EEC (AIMDD), or EU IVD Directive 98/79/EC (IVDD).

5 For example, a mandatory application audit will be conducted once the sponsor lodges an Application for Inclusion of any Class III, AIMD, and some Class IIb devices covered by EC Certificates in the ARTG with the TGA.

6 For example, EC certificates cannot be used to support applications for market authorisation (ARTG inclusion) for devices which include medicines or contain materials of animal, microbial or recombinant origin, and/or Class 4 IVDs, which must be supported by a TGA conformity assessment certificate.

7 This excludes ARTG entries for low risk Class I medical devices, which are self-certified by manufacturers and do not require a conformity assessment certification.

TGA officers are active in the IMDRF Management Committee and are also participants in the IMDRF working groups. These activities promote deeper collaboration among medical device regulators and also create greater alignment between these agencies.

The TGA will continue to work with our international counterparts through these existing arrangements, supporting a continued movement towards globally harmonised medical device regulation. The criteria proposed in this paper are intended to allow a framework where the work of similar overseas medical device regulators can be recognised within the Australian jurisdiction.

MDSAP

The Medical Device Single Audit Program (MDSAP) is a flagship application of the work of the IMDRF for an operational program that pools resources and encourages the convergence of regulatory requirements of the participating Regulatory Authorities. MDSAP is designed to produce evidence that may be used for market authorisation decisions with the MDSAP evidence demonstrating the QMS requirements of the participating regulatory authorities (Australia, Brazil, Canada, Japan and the USA). The pilot of this single audit-program was completed at the end of 2016, with MDSAP now in a transition phase which will conclude in 2019.

During the transition phase the participating regulators are using the MDSAP outputs as evidence of regulatory compliance within their respective regulatory environments. The MDSAP FAQ number 34[8] provides more detail for each of the regulators in the transition period. Since MDSAP produces evidence of regulatory compliance it can be used as a basis for comparability for QMS requirements.

Cooperative agreements

In addition to participation in IMDRF and MDSAP, the TGA is also involved in information-sharing and other activities with a number of overseas regulators. The TGA has existing agreements and Memoranda of Understanding (MOUs) with many of these agencies, including the following IMDRF members (including European member states):

- Brazil
- Canada
- France
- Germany
- Ireland
- Japan
- Singapore
- United Kingdom
- United States of America

Under the current Australian therapeutic goods legislation, these cooperative relationships underpin the TGA's ability to release and share information. This is critical to protecting the health and safety of the populations of our respective countries. These written agreements

[8] US FDA website, Resources for You: Questions and Answers on the Medical Device Audit Program December 16, 2016 https://www.fda.gov/downloads/MedicalDevices/InternationalPrograms/MDSAPPilot/UCM430563.pdf

outline a history of international cooperation that has been used to develop an understanding of each agency's regulatory practices and systems.

Use of international standards

It is expected that manufacturers demonstrate compliance with the Essential Principles by meeting a recognised standard published by an Australian or International Standards Agency, a Pharmacopoeia, or a similar standard. Where an overseas regulatory approval is based on the same or comparable standards the assessment undertaken is more likely to also be of use in the Australian context. The criteria proposed in this consultation paper are not intended to revisit this, but instead build on this work which has already been accomplished.

A wide range of ISO standards are applicable to medical devices, some broadly relevant and others relevant to specific device streams. There may also be country or region specific versions of standards which may apply (for example, an Australian standard or European standard may be used). ISO standards which we would expect to see considered by overseas regulators include (but are not limited to):

Ref. number	Title
ISO 13485	Quality Management Systems (QMS)
ISO 14155	Good Clinical Practice
ISO 14971	Application of risk management to medical devices
ISO 11979-7	Ophthalmic implants - intraocular lenses
ISO 5840-1 ISO 5840-2 ISO 5840-3	Cardiovascular implants - cardiac valve prostheses
ISO 14708	Implants for surgery - Active implantable medical devices
ISO 14117	Electromagnetic compatibility test protocols for active implantable medical devices

Scope and context

Are there additional issues which should be considered in developing this proposal?

Use of overseas regulatory approvals

The regulatory regimes of international jurisdictions differ, and assessments under each framework are aimed to satisfy that country's particular regulatory requirements. The capacity for the TGA to use assessments by comparable overseas regulators or third parties they designate will vary based on the degree to which the assessment can be repurposed to demonstrate compliance with the Australian regulatory framework. A brief introduction to the Australian regulatory framework for medical devices is included at **Attachment A**.

Proposed use of overseas assessments

The primary objective of this proposal is to identify comparable overseas regulators for either:

- use of approvals from comparable overseas regulators as the evidence of the regulatory compliance for the purposes of applications for inclusion of medical devices in the ARTG; or
- work-sharing with comparable overseas regulators to progress applications lodged in parallel in the two (or more) jurisdictions.

Use of overseas approvals to support inclusion in the ARTG

This would avoid the need for duplicate assessments where TGA has not issued a conformity assessment certificate. This is already the case in practice when relying on conformity assessment certification (EC Certificates) from European notified bodies. As applies now when relying on European certification, this would not apply for inclusion applications for those very high risk devices which require TGA conformity assessment.[9]

To use overseas regulatory approvals, the assessments undertaken by the regulator or designated body will need to be mapped against the Australian requirements to ensure:

- safety, quality and performance are demonstrated to meet the Australian requirements for compliance against the Essential Principles (noting that overseas jurisdictions do not assess against 'Essential Principles', but do assess safety, quality and performance);
- comparable classification of the medical device, so that the rigour of the assessment is appropriate to the Australian categorisation of the risk of the medical device.

This is typically fairly straightforward in respect of certificates issued by a European notified Body, given the close parallels between the Australian and European regulatory frameworks. The extent that this is practicable for assessments by other overseas regulators will vary based on:

- **comparability** of the overseas regulator, as assessed against the proposed criteria outlined below; and
- the scope and practicality of the additional assessment required to bridge any **gap** between the evaluation of evidence in the overseas assessment and the evaluation of evidence required to support a decision against the Australian regulatory framework.

Work-sharing with comparable overseas regulators

Work-sharing is where a medical device application dossier is submitted simultaneously to two (or more) regulators and is then jointly assessed. This would apply to conformity assessment

[9] Therapeutic Goods (Medical Devices) Regulations 2002 Part 4, Regulation 4.1 requires TGA conformity assessment certification for medical devices which include medicines, materials of recombinant, human or animal origin, of Class 4 IVDs).

applications, as applications for inclusion pre-suppose conformity assessment (or an equivalent regulatory approval as outlined above) has already been completed for the device.

Again the extent that this is practicable for assessments by other overseas regulators will vary based on:

- the **comparability** of the overseas regulator, as assessed against the proposed criteria outlined below; and
- the **willingness** of and any **logistical constrains** in the overseas regulator participating in work-sharing.

It should be noted that use of all or part of completed assessments from overseas regulators already occurs in the conformity assessment context, where reports are provided by applicants. In addition, a number TGA conformity assessment applications are for combination products (those containing medicines, or materials of animal, microbial or recombinant origins). In the context of work sharing it may be relevant to consider overseas assessments for these elements.

Discussion

Gap analysis

Australian specific requirements, such as local recall and adverse event reporting procedures etc., would not usually be covered by an assessment by the overseas regulator[10] (or their designated third party assessment body). Additional evidence may be required in addition to the overseas regulatory approval to address such gaps. The way in which the overseas assessment is structured and undertaken may also complicate using reports to demonstrate compliance with Australian regulations.

For use of overseas approvals, the extent of the gap between the overseas approval and the additional information required by TGA to establish compliance with the regulatory framework will be critical. If the additional information to be assessed by the TGA is too extensive it will be impractical to allow use of the overseas approval, as the TGA would effectively be undertaking an abridged conformity assessment (without the corresponding fee). As the TGA's pre-market activity is cost recovered on a fee for service basis, it would be inappropriate to cross-subsidise extensive additional assessment in the application for inclusion process.

Such gaps, and how to bridge them, will also need to be clearly articulated in guidance, to allow applicants to judge whether to apply for inclusion on the basis of such evidence.

For work-sharing, pre-submission discussions between regulators will be critical to establishing a willingness to cooperate on the assessment. The specifics of work-sharing would need to be finalised early in the assessment process to allow an appropriate abridgement of fees by one or both regulators. Any country specific requirements would be undertaken by appropriate regulator.

Application audits

At present the TGA may audit any application for inclusion in the ARTG, and must audit applications for high risk devices where a device is not supported by a TGA conformity assessment certificate. This application audit process manages the risk of using overseas approvals where TGA otherwise has no oversight of the overseas assessment process, providing a mechanism to assure that the approval is appropriate for the Australian context.

10 Unless it is an MDSAP audit that is required to specifically identify and audit the effectiveness of the arrangements with an Australian Sponsor for Australian recall and adverse event reporting.

It is proposed this application audit requirement would apply when relying on the approval of a high risk device from a comparable overseas regulator. The application audit process is currently used for such devices when an applicant is relying on European notified body conformity assessment certification (EC Certificates). The focus of application audits may vary based on the comparable overseas regulator, so address differences in regulatory frameworks.

There is a parallel MMDR proposal to establish Australian conformity assessment bodies that are to be directly designated by the TGA.[11] In that proposal, applications for inclusion in the ARTG, that rely on certificates from a conformity assessment body(ies) designated by TGA, would not require a compulsory application audit even for high risk devices. The associated risk would be managed through the process of designating the conformity assessment body, rather than by auditing individual applications for inclusion in the ARTG. TGA would continue to have the discretion to audit any ARTG inclusion application, and some very high risk devices would continue to require a TGA conformity assessment certificate (that may require both a product assessment and an on-site QMS audit by the TGA).

Timing and assessment of conformity assessment applications

For work sharing, a joint proposal would need to be submitted by related companies in each country with the express consent of each other to apply the work sharing process. The process would be based on each agency taking responsibility for the assessment of discrete elements of the application. For example, clinical evidence may be examined by one regulator, while bio-materials are assessed by another. At the completion of the assessments, reports would be exchanged directly between the agencies. Each agency then follows their own independent decision-making processes, including the right to refer to expert advisory bodies.

In practice this would operate similar to the process for abridging a conformity assessment application. The key difference is that the component assessments would be developed in parallel by the different regulators during the time of the application assessment, rather than by using prior assessments completed by other regulators that would be submitted to the TGA at the time of the application. It should be noted that work sharing would only occur at the request of the applicant and would be subject to agreement by the comparable regulator, on an application by application basis.

Assessment procedures and guidance

As discussed above, the capacity to use overseas regulator assessments depends both on the extent to which the overseas regulator is 'comparable' as assessed against the criteria, and the practical capacity to bridge the gap between the overseas assessment and the Australian regulatory requirements.

In order to implement the use of approvals from comparable overseas regulators as the evidence for applications for inclusion of the medical device in the ARTG it will be necessary to assess comparability of the regulator and undertake an analysis of a comparable overseas regulator's assessment process to generate a standard process for TGA's assessment of applications relying on such evidence. Review of the assessment process is expected to include:

- review of the overseas regulatory framework, including its objectives, processes, the requisite competencies to conduct assessments and the suitability of any outputs for use as objective evidence for decision making.
- an analysis of sample assessment reports

[11] Consultation on this proposal was recently undertaken. For details refer to the consultation paper available on the TGA website https://www.tga.gov.au/consultation/consultation-designation-australian-conformity-assessment-bodies-medical-devices-implementation

- gap analysis comparing the overseas and Australian regulatory requirement
- identifying and documenting the information required to be assessed for the applications for ARTG inclusions.

Implementation mechanism

Criteria for assessing the comparability of an overseas regulator would be the same, whether for use of overseas approvals to support inclusion in the ARTG or work-sharing, although their application for different jurisdictions may vary. For example the information and assurance to support use of overseas approvals to support inclusion in the ARTG may be in place for a particular regulator, but that regulator may be unwilling to participate in work-sharing arrangements.

Regulatory list of comparable overseas regulators

Once an overseas regulator has been assessed as both comparable and the use of their assessments practically appropriate, they would be included as a 'comparable overseas regulator' in a list published as a legislative instrument on the TGA website. This list may need to be updated regularly. It would include overseas regulators who directly undertake assessments and those regulators who designate third party assessment bodies to undertake assessments on their behalf (such as European regulators, which designate European notified bodies in their jurisdictions).

In practice the arrangements for the use of overseas approvals, to support inclusion in the ARTG, need to be clear to applicants to allow them to judge whether they have sufficient information to support their application. For that reason the approach proposed above would also apply for the use of overseas approvals to support inclusion in the ARTG. The list would also provide an indication of regulators which would be favourably considered for work-sharing, but the capacity to engage in work-sharing would need to be assessed on an application by application basis. Any conformity assessment applicant wishing to be considered for work-sharing should approach TGA on options as part of pre-submission engagement.

Possible scope exclusions

There are some differences between Australian and European requirements, for example some devices are classified differently. This means that European notified body certification issued in relation to the device that is classified lower in Europe than in Australia cannot be used in Australia.[12] These exclusions may also apply for overseas approvals of particular medical devices where particular assessment processes undertaken by the regulators are not sufficiently comparable to Australian assessment processes (for example, the capacity to rely on the US FDA's Premarket Approval (PMA) and Premarket Notification 510k processes may differ).

Assessment of comparability of a regulator against the criteria and the gap analysis to develop standard operating procedures (SOPs) and guidance is a significant investment of TGA resources. Undertaking this analysis may be of marginal value in respect of some overseas regulators; such as where few applicants are expected from sponsors who wish to rely on an approval from a particular overseas regulator. TGA may also be unable to satisfactorily complete such analysis, where details of the assessment process are not sufficiently transparent or a sufficient sample of assessment reports are not available to TGA. Hence, meeting the criteria for

12 For example, the Australian definition of the central circulatory system extends beyond the current EU MDD definition to include the common iliac arteries. As a result some devices classified as Class III in Australia have a lower classification in Europe. A European conformity assessment certification appropriate for a Class IIb medical device may not be sufficient to support inclusion of the device in the ARTG as a Class III, and consequently a TGA conformity assessment certificate may be required.

a comparable overseas regulator is necessary, but may not be a sufficient basis to formally recognise an overseas regulator as a comparable overseas regulator.

It should also be noted that it is unlikely that work-sharing will be possible with European notified bodies (or other commercial bodies designated by regulators to undertake assessments). International cooperative agreements operate between government regulators rather than commercial organisations. Even where this can be overcome, it is unlikely a commercial organisation will wish to participate in such an arrangement when it is likely to be to their commercial detriment.

Expected recognition of overseas regulators

- At this stage, in line with the criteria below, it is anticipated that only overseas regulators which are participating members of the IMDRF (members of the management committee) would be evaluated against criteria for inclusion in the list of comparable overseas regulators. For use of overseas approvals to support inclusion in the ARTG: Analysis of overseas regulators would be considered on a regulator by regulator basis, taking into account:
  - the resources required in TGA to undertake the assessment and develop the assessment material and guidance required to implement use of the overseas approval, expected utilisation of approvals from the regulator, and accessibility of sample assessment reports to support analysis.
  - consultation would be undertaken with the requesting individual or organisations and industry representatives (via the Regulatory and Technical Consultative Forum) prior to deciding whether to proceed with analysis.
- For work-sharing: Analysis of overseas regulators would be considered on an application by application basis, taking into account the:
  - comparability of the assessment required by each regulator, such as component assessments which both jurisdictions agree need to be undertaken; and
  - willingness of the overseas regulator to participate, and the existence and scope of cooperative agreements, to facilitate work-sharing.

Use of overseas regulatory approvals

- **Is the proposed use of a list of comparable overseas regulators in a legislative instrument published on the TGA website, rather than the criteria, appropriate?**
- **Are there additional issues which should be addressed in the regulations, assessment procedures or guidance?**
- **Are there other overseas regulators you would expect to be included, beyond IMDRF management committee members?**

Work-sharing

- **Is an 'application by application' arrangement for work- sharing appropriate, or can you suggest how a more systematic approach might operate?**

Proposed criteria

Taking into account the various factors outlined in the MMDR Report (at Recommendation 17) the following criteria are proposed:

1. Comparability of the regulatory framework of the overseas regulator
2. IMDRF membership
3. Life cycle approach and post market vigilance
4. Communication and cooperation with overseas regulators
5. Expertise of the overseas regulator

1. Comparability of the regulatory framework

Scope

- **Does the overseas regulator take into account the same or similar regulatory objectives and other factors that are prescribed in the TGA's legislation and regulations (e.g. is the definition of a medical device substantially the same)?**
- **Does it take into account objectives that are excluded in the Australian legislation, for example additional policy objectives such as industry development or environmental protection?**
- **Does the overseas regulator provide complete (un-redacted) reports and is supporting scientific data used in assessments available if necessary?**

The scope, definitions, and required approaches within the TGA framework reflect the policy intentions of government. These may not always line up with the corresponding legislative framework in other countries. Differences can be as fundamental as the definitions of what is actually regulated, the issues to be considered, the risks that are to be assessed in the regulation and the actual process to be used in the management of that risk. These differences may not preclude use of overseas regulatory assessments; however the TGA will need to take any differences into account when contemplating the use of international assessments.

It is important that the use of international assessments is done in a manner that is consistent with the legal construct of the TGA to ensure that the legally accountable regulatory decisions taken by TGA's delegates (decision makers) are not compromised and hence open to successful challenge. A loss of such a challenge may lead to a loss of confidence in the regulator. Consequently, the overseas regulator should have a transparent system for regulating therapeutic goods, including competent and robust assessment processes and legal accountability.

In relation to this criterion, the TGA should ensure that it has a good understanding of the approaches used by the particular country and satisfy itself that it reflects best practice (including on factors such as safety, quality, objectivity, competence and conflict of interest).

This framework will need to take into account legislative requirements in both countries (including matters such as confidentiality, intellectual property, transparency and conflict of interest). The framework will also need to include provision for access to full, un-redacted reports (and relevant scientific data), and the ability to seek clarification on those reports with the overseas regulator.

It should be noted that redacted reports are not adequate for assessing compliance with Australian requirements. When relying on overseas approvals it is the responsibility of the applicant to ensure that un-redacted reports are available to support their application.

Operational alignment

- **Is there a clearly defined framework within which assessment reports are prepared by an overseas regulator?**
- **Does the overseas regulator require or allow for compliance with international standards in assessing medical devices?**
- **Does the overseas regulator routinely provide its assessment reports in English and are these available to the relevant sponsor?**

Understanding the way in which assessments are undertaken by overseas regulators will be important in providing assurance to TGA in relying on such assessments.

The adoption of international standards is a key mechanism for ensuring that the data requirements and assessments reflect agreed international best practice. Applicants under the Australian regulatory framework are expected to rely on standards to demonstrate compliance with the Essential Principles, although TGA does not mandate such compliance as the only way to demonstrate this. Any differences in how international or more localised standards are relied upon will need to be understood to best make use of overseas assessments.

Reporting in English is necessary to ensure that neither time nor accuracy is lost in translation. For the same reasons, it is important that TGA evaluators, where required, are able to communicate in English with those who conduct the assessments, particularly where work-sharing is undertaken. The Australian sponsor must also be able to access assessment reports to allow them to be provided to TGA and/or to respond to TGA queries (even where reports may be sourced directly from the overseas regulator). In particular circumstances certified translations may also be acceptable, such as where regulatory staff are able to communicate effectively in English, as is the case for many European countries.

2. IMDRF membership

- **Is the overseas regulator a participating member of the IMDRF (i.e. a member of the IMDRF management committee)?**

"The mission of the IMDRF is to strategically accelerate international medical device regulatory convergence to promote an efficient and effective regulatory model for medical devices that is responsive to emerging challenges in the sector while protecting and maximizing public health and safety."[13]

Active participation on the IMDRF demonstrates a commitment to work towards international regulatory **convergence**, and indicates an acceptance (at varying levels) of the GHTF regulatory guidance material on which the IMDRF work is based. Participation in the IMDRF provides assurance that future regulatory changes in a particular country are likely to be consistent with working towards international harmonisation of medical device regulation.

[13] http://www.imdrf.org/docs/imdrf/final/procedural/imdrf-proc-150102-terms-of-reference.pdf

3. Life cycle approach and post-market vigilance

- **Does the overseas regulatory framework apply across the life cycle of medical devices?**
- **Does the overseas regulator have a robust approach to post-market vigilance?**

Under the Australian regulatory framework, once a device is approved, manufacturers are expected to continue to monitor the performance and safety of devices, and ensure continued compliance with the Essential Principles. This surveillance program is part of the quality management system aspect of their conformity assessment, and it is expected it will be periodically checked by the certifying body. While an overseas regulator may not be focused on ongoing application of the 'conformity assessment procedure', regulation based on a life cycle regulatory approach (rather than a simple point in time assessment) and an ongoing post-market surveillance program would be a necessary requirement. Comparability of regulatory actions, such as recall processes and the suspension or cancellation of marketing approval, would also need to be considered.

4. Communication and cooperation with overseas regulators

- **Do the overseas regulator and TGA have communication and/or cooperative arrangements in place?**
- **Is there a framework within which assessment reports prepared by overseas regulators, as well as surveillance signals, regulatory actions etc., can be shared with the TGA (and vice versa)?**

TGA has arrangements in place with a range of overseas regulators, such as Memorandums of Understanding (MOUs), to facilitate effective communication and the exchange of information.

Product assessment and QMS audit reports are intended to be a *prima facie* (sufficient) evidence to demonstrate fulfilment of regulatory requirements, which typically involves the assessor or auditor to take into account Australian regulatory requirements. While there are other methods to obtain the necessary work product to support assessment, such as provision of reports by the applicant, the existence and scope of an MOU, Statement of Cooperation (SoC) or similar arrangement will be a relevant consideration. There is an opportunity within these arrangements for the content of regulatory reporting to be agreed by the participants.

For work-sharing, regulators may also be constrained from sharing information due to legislative confidentiality requirements. The existence of cooperative arrangement means the capacity and mechanisms for the regulators sharing information will be clearly established.

The existence of such cooperative arrangements is also important in respect of sharing the findings of the regulator's post-market vigilance and surveillance activities, up to and including suspension or cancellation of marketing approval by the regulator. While sponsors of medical devices are required to advise TGA of overseas regulatory actions, independent communication with other regulators mitigates the risk of sponsors failing to provide accurate and timely advice on these issues.

IMDRF membership indicates a shared commitment in working towards a globally harmonised medical device regulatory system. Periodic IMDRF meetings also provide a forum for regular contact, and participation in international forums creates confidence between regulators, supporting cooperation and mutual understanding.

5. Expertise of the overseas regulator

- **Does the overseas regulator have experience in conducting product evaluations and QMS assessments, by competent resources, which would satisfy the expectations for internationally agreed best practice, both generally and for particular types of medical devices?**

The overseas regulator will need to have experience in conducting full *de novo* assessments of the type of applications that are of interest to the TGA. The demonstrable competence (knowledge, skills and experience) of the expert resources used in undertaking assessment of particular technologies is a necessary consideration.

Importantly, the regulator should have established processes to evaluate dossiers containing scientific data, a system of peer review, and referral for independent expert advice in relation to their assessments.

Proposed criteria

- **Are the proposed criteria appropriate? Are there additional issues within particular criteria which need to be considered?**
- **Are the criteria appropriate for both use of overseas approvals and work-sharing?**
- **Are there additional criteria which should be included on consideration of comparable overseas regulators?**

Proposed implementation

Legislative amendments

Legislative amendment to the *Therapeutic Goods Act 1989* (the Act) are expected to be necessary to implement these changes. The changes will primarily provide for the inclusion of a list of comparable overseas regulators in the medical device regulatory framework.

Changes to fees and charges need to be consistent with cost recovery principles.

Based on the outcome of this consultation and the passage of legislation, the regulatory amendments will be developed during 2017, for a scheduled 1 January 2018 commencement.

Operational arrangements

Policy, procedures, guidance and operational supports (information technology, etc.) to support the operation will be required. It should be noted that, for use of overseas approvals to support

inclusion in the ARTG, this is expected to include changes to the existing manufacturers' evidence processes and IT systems.

Based on the outcomes of this consultation, these would also be developed throughout 2017, to be in place in anticipation of the scheduled 1 January 2018 commencement.

Proposed implementation

- **Are there any gaps in the proposed approach to implementation?**
- **In addition to any feedback on specific aspects of the proposed approach outlined above, do you have broader comments on the proposal?**

Attachments

Attachment A - TGA assessment of medical devices

The regulatory framework for medical devices spans the life cycle for these products. Medical devices are assessed, in line with their intended purpose and risk based classification, against Essential Principles relating to the safety and performance of medical devices. This process includes:

- **Pre-market assessment:** Conformity assessment
- **Market authorisation:** Inclusion in the Australian Register of Therapeutic Goods (ARTG)
- **Post-market monitoring:** Continuing compliance with all regulatory, safety and performance requirements and standards.

These concepts are outlined below.

What is a medical device?

Medical devices are defined by section 41BD of the *Therapeutic Goods Act 1989*[14]. In summary, these are devices which are used on humans, have therapeutic benefits or modify anatomy, and generally have a physical, mechanical or chemical effect on the body or are used to measure or monitor functions of the body. Implantable prostheses are medical devices[15].

Under the *Therapeutic Goods Act 1989* a 'kind of medical device' must be included in the Australian Register of Therapeutic Goods (ARTG) prior to supply in Australia, unless an exemption applies[16]. For all but the lowest risk Class I medical devices this includes a premarket assessment by the TGA before the device is authorised to be supplied in Australia[17]. The rigour of this assessment is based on the intended use and risk classification of the device.

Kind of device

For high risk devices (Class III and AIMD) 'kind of device' is a fairly narrow grouping restricted to a single Unique Product Identifier (UPI), typically covering design variations of a single device such as devices with different length, width, shape, etc. to provide for the anatomical differences between patients (defined in the regulations as variants).

It should be noted that a 'kind of medical device' is a broader concept for Class IIb and lower classifications, and covers a range of similar products which have the same sponsor, manufacturer, classification and are described by the same Global Medical Device Nomenclature (GMDN)[18] code. For example, a single ARTG entry may cover a range of different models or brands of similar devices, such as the multiple variations of intravenous infusion sets from the same manufacturer and sponsor.

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14 *Therapeutic Goods Act 1989*

15 Due to their function to replace and/or modify the human anatomy and/or a physiological process

16 For example, an exemption applies for custom made medical devices, which are regulated under the *Therapeutic Goods Act 1989* but exempt from the requirement to include them in the ARTG.

17 Given the low risk of Class I medical devices (except those which include a measuring function or are supplied sterile) and some Class 1 IVD devices, conformity assessment procedures are self-assessed by the manufacturer, and medical devices are included in the ARTG without further TGA assessment.

18 The Global Medical Device Nomenclature (GMDN) is an international system used to identify medical devices. The TGA use the GMDN system as one of the criteria to distinguish one kind of medical device from another.

New products may be supplied under an appropriate existing ARTG entry without further clearance by or notification to the TGA (unless it is required under the conditions of ARTG inclusions or when information entered on the ARTG in relation to the device should be corrected). However, any new device which fits within the 'kind' must meet the requirements of the conformity assessment procedures implemented by the manufacturer in relation to that kind (and in line with the risk of the device will be assessed or monitored via the ongoing certification by either TGA or a European notified body).

Essential Principles

Medical devices must conform to the Essential Principles, with the rigour of the 'conformity assessment'[19] to the Essential Principles varying in line with the risk of the medical device, as indicated by the classification.

The Essential Principles[20] set out the requirements relating to the safety and performance characteristics of medical devices. There are six general Essential Principles that apply to all devices – relating to health and safety, including long term safety, with benefits outweighing the risks - and a further nine Essential Principles about design and construction that apply to devices on a case-by-case basis. There are:

Part 1 – General Principles

6. Use of medical devices not to compromise health and safety
7. Design and construction of medical devices to conform with safety principles
8. Medical devices to be suitable for intended purpose
9. Long-term safety
10. Medical devices not to be adversely affected by transport or storage
11. Benefits of medical devices to outweigh any undesirable effects

Part 2 - Principles about design and construction

12. Chemical, physical and biological properties
13. Infection and microbial contamination
14. Construction and environmental properties
15. Medical devices with a measuring function
16. Protection against radiation
17. Medical devices connected to or equipped with an energy source
18. Information to be provided with medical devices
19. Clinical evidence
20. Principles applying to IVD medical devices only

This principles based regulatory framework caters for technological advances and changes in the development of new medical devices and provides flexibility for manufacturers. It does not

19 Conformity assessment procedures are outlined in Part 3 of the Therapeutic Goods (Medical Devices) Regulations 2002.

20 The Essential Principles are prescribed in Schedule 1 of the Therapeutic Goods (Medical Devices) Regulations 2002.

mandate the means by which a manufacturer must prove that they have met the Essential Principles.

Classification of medical devices

The risk management approach underpins the classification system for medical devices. Manufacturers classify the medical device according to its intended purpose and the degree of risk involved for the patient, the user and the environment. The device classifications are determined using a set of rules[21] that take into account the degree of invasiveness in the human body, the duration and location of use and whether the device relies on a source of energy other than the body or gravity. Multiple classification rules may apply for any given medical device, and the device will be classified at the highest applicable classification.

The classification rules for medical devices and IVDs are summarised in the following tables:

Classification of medical devices

Class	Risk	Examples
Class I	Low	Surgical retractors, tongue depressors
Class I – supplied sterile Class I – incorporating a measuring function	Low-medium	Sterile bandages, drainage bags
Class IIa		Hypodermic needles, suction unit
Class IIb	Medium-high	Lung ventilator, surgical meshes
Class III	High	Heart valves, devices containing medicines or tissues, cells or substances of animal, biological or microbiological origin
AIMD (Active Implantable Medical Devices)		Implantable defibrillator

21 The classification rules for medical devices are prescribed in Schedule 2 of the Therapeutic Goods (Medical Devices) Regulations 2002.

Classification of IVDs

Class	Risk	Examples
Class 1 IVD	No public health risk or low personal risk	Instrumentation and analysers (e.g., glucose meter). Microbiological culture media.
Class 2 IVD	Low public health risk or moderate personal risk	Pregnancy self-testing kit. Liver function tests.
Class 3 IVD	Moderate public health risk or high personal risk	Test to detect the presence or exposure to a sexually transmitted agent such as C. trachomatis or N. gonorrhoea.
Class 4 IVD	High public health risk	Assay intended for the clinical diagnosis of HIV. Assay intended for screening blood donations for Hepatitis C virus.

Pre-market assessment - Conformity assessment of medical devices, including IVDs

Conformity assessment is the systematic and ongoing examination by the manufacturer of evidence and procedures to determine that the safety of a medical device is acceptable and the device performs as intended and, therefore, conforms to the Essential Principles.

To be included in the ARTG an appropriate conformity assessment procedure must have been applied to the medical device. This is usually demonstrated by relying on certification issued by a conformity assessment body (such as the TGA or a European notified body).

The level of assessment required is commensurate with the level and nature of the risks posed by the device to the patient, ranging from manufacturer self-assessment for low risk devices through to an assessment of the manufacturer's quality management system and examination of the design of the specific device by a conformity assessment body, for the highest risk devices[22].

Manufacturers are required to hold a TGA conformity assessment certificate in relation to specified highest risk medical devices. These are those medical devices that contain medicines or tissues, cells or substances of animal, biological or microbiological origin and Class 4 IVDs and are identified in the Regulations.[23]

For other medical devices, and given the close parallels between the European and Australian regulatory frameworks, the TGA generally accepts conformity assessment certification (EC Certificates) from European notified bodies issued under the European Medical Device Directives[24].

22 Conformity assessment procedures are outlined in Schedule 3 of the Therapeutic Goods (Medical Devices) Regulations 2002.

23 Therapeutic Goods (Medical Devices) Regulations - Regulation 4.1

24 European Directive 93/42/EEC on Medical Devices or Directive 90/385/EEC on Active Implantable Medical Devices

Market authorisation - Inclusion of medical devices in the ARTG

Once conformity assessment certification is obtained from an appropriate conformity assessment body, an application to include the medical device in the ARTG can be made. The applicant must be an Australian entity, and usually is an Australian importer of overseas manufactured medical devices. Applicants must have a relationship with the manufacturer to enable them to fulfil their regulatory obligations.

The degree of rigour of the assessment conducted by the TGA at the point of application for ARTG inclusion depends on the intended use and risk classification of the device and the source of the conformity assessment certification. The TGA may approve the inclusion of a device in the ARTG based solely on the application received, or may require a more detailed audit of the application involving a desk top review of information such as the labelling, instructions for use, technical and advertising materials for the device, and possibly a review of the clinical evidence and risk management documentation for the device.

The scope of any application audit will depend largely on the issues identified by the TGA as requiring further scrutiny. In most cases high risk devices (Class III, AIMDs), selected Class IIb, and some IVD medical devices, are subject to mandatory application audits[25] where the manufacturers' conformity assessment procedures have not been assessed by the TGA.

Post-market assessment of medical devices and IVDs

Maintenance of conformity assessment

Once a device is approved manufacturers are expected to continue to monitor the performance and safety of devices, and ensure continued compliance with the Essential Principles. This surveillance program is part of the quality management system aspect of their conformity assessment, and will be periodically checked by the certifying body (whether this is the TGA or a European notified body). These surveillance programs should be appropriate to the use and risks of the device.

The data generated from safety and adverse event reports and complaints, newly identified risks, literature, any updated or new clinical investigations, significant regulatory actions and formal surveillance activities such as registries should be used to review the performance, safety and benefit-risk assessment of the device.

TGA post market vigilance and monitoring

The medical device regulatory framework includes provision for post-market monitoring by the TGA, including:

- risk assessment and investigation of medical device adverse event and complaint reports
- checking evidence of conformity against the Essential Principles
- conducting periodic audits of a manufacturers' quality management system and technical documentation
- imposing specific requirements for manufacturers and sponsors to report, within specified timeframes, adverse incidents involving their medical devices.

25 Regulation 5.3 of the Therapeutic Goods (Medical Devices) Regulations 2002 outlines which medical devices MUST be selected for audit, and a fee will apply for these audits. TGA may select any application for audit, but no fee applies when the audit is at TGA's discretion.

Post-market monitoring by the TGA is carried out to ensure the ongoing regulatory compliance and safety of medical devices supplied to the Australian market.

In support of the TGA's post-market monitoring activities, the sponsor of a medical device has ongoing responsibilities once a device has been included in the ARTG. These statutory responsibilities include that the sponsor must report to the TGA adverse incidents, overseas regulatory actions, and the results of investigations undertaken by the manufacturer such as further clinical studies, reviews of adverse events, etc. The sponsor must also maintain distribution records.

All adverse event reports or complaints received by the TGA are entered into a database, and a risk assessment is undertaken by a panel of clinicians and scientists within the TGA to determine if investigation is required. External expert advice may be sought during an investigation.

The outcomes of the TGA's investigations may result in product recovery (recalls); hazard and safety alerts; product modification/improvement by a manufacturer; or surveillance audits of manufacturing sites.

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Reference/Publication # D17-312985