Changes to Premarket Assessment Requirements for Medical Devices: Regulatory Impact Statement

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Background

For the past four years, the Therapeutic Goods Administration (TGA) has been proactive in reforming many aspects of its function as Australia’s principal regulator of therapeutic goods. These reform consultations have included options to reform the advertising arrangements for therapeutic goods, the premarket approval process for medical devices, and the evaluation of complementary medicines. The emphasis on engaging all aspects of the community around these issues is to be commended, and we welcome the opportunity to comment on the reforms put forward in the present regulation impact statement (RIS) on the preapproval of medical devices.

As recent research and Senate inquiries have indicated, there is a need to improve the regulation of medical devices in Australia.[1, 2] The debate around medical device reforms has focussed primarily on high-risk hip and breast implants, due to the large impact that failed implantable devices have had in both Australia and overseas.[3] However, there are a number of issues which relate to breast cancer imaging devices that are relevant to this discussion of regulatory improvement.

A number of new and emerging technologies used for breast cancer screening and diagnosis have entered the Australian market in recent years, including electrical impedance scanning, digital infrared thermal imaging, and electronic palpation imaging, also referred to as computerised breast imaging. These devices are funded out-of-pocket, do not require a referral from a doctor, and are promoted directly towards consumers as safe and effective solutions for breast cancer screening and diagnosis - applications for which they have not received TGA certification. In response to these advertising claims the devices have drawn considerable attention from various interest groups,
including the Australian Competition and Consumer Commission, and the National Health and Medical Research Council, that have questioned their safety and performance as breast imaging tools.[4-10] This situation is known to the TGA, as several devices were removed from the register in 2011, following a series of complaints raised with the Complaints Resolution Panel (CRP).[11]

In 2011, we conducted a systematic review that examined the evidence base to support these devices for breast cancer screening and diagnosis. The findings of our review indicate that there is currently insufficient evidence to recommend the use of these technologies for breast cancer screening, and the high level of variability among studies of symptomatic women limits their utility as diagnostic tools as well.[12] Despite having limited, variable quality evidence for screening and diagnosis, these devices are advertised for these indications in Australia, the United States, Canada, and the United Kingdom.[4, 13-15]

The present consultation presents a unique opportunity for members of the breast cancer community to provide input into the manner in which new breast imaging devices may be regulated in the future. In order to ensure that the breast cancer community is represented in this reform process, we conducted semi-structured interviews with members of national and state-based, not-for-profit organisations involved in breast cancer imaging research (n=4), patient advocacy (n=7), and prevention/screening (n=5) between January and March 2013. In total, we interviewed 16 stakeholders from within the breast cancer community around the TGA’s proposed options for reform to both the premarket approval process for medical devices,[16] as well as the proposed changes to the regulation of therapeutic goods advertising [17]. In this submission, we summarise the responses around the proposed changes to the premarket regulation of medical devices outlined in the RIS.

**Proposal A: Increased scrutiny of conformity assessment as part of mandatory application audits prior to ARTG inclusion of high risk devices**

Proposal A was not part of our interview process, as emerging breast imaging devices have been registered on the Australian Register of Therapeutic Goods (ARTG) under the low risk category, Medical Device Included Class Ila (ARTG entry numbers 152697, 141616). As such we have no comment from participants on this option for reform. We would, however, like to add general comments on the issue of conformity assessment and risk classification.
The risk-category that determines the level of pre-market evaluation a medical device faces during conformity assessment is currently determined by the manufacturer of the device when applying for certification.[18] However, as we have observed in the case of emerging breast imaging devices, the intended use of a listed device on the ARTG is often different from the practical application of the device. For example, the intended use of one imaging device currently listed on the ARTG, as defined by the manufacturer, states that the device:

“... is intended to document lesions as identified during a clinical breast exam by producing an accumulated image for each of the areas that contain a lesion. The device should not be used for clinical decision-making.”[ARTG entry number 141616]

However, on the manufacturer’s website it states that the device:

“... is a unique digital sensing device that assists a physician or other trained healthcare professional in screening for breast cancer during routine exams”. [19]

In this instance, if the device was registered for its practical use, i.e. breast screening, rather than its “intended use” as listed on the ARTG entry, then the device should have been registered in a higher risk category to account for the potential harm the device can cause through false-positive and false-negative test results. This particular example is less explicit than advertising material presented in the past, as the manufacturer altered online claims due to a complaint raised to the CRP in 2010.[9] However, this is merely one example of an issue that has been identified throughout the industry, and may be occurring with an unknown number of other classes of listed products. Furthermore, if the TGA were to accept FDA clearance for low-risk devices, as has been discussed in the recent reform consultations, it would have identified that the thermography and impedance devices from the US received a high-risk, Class III classification for use a breast cancer imaging, and can only be accessed via prescription if used as a standalone breast screening or diagnostic tool.[20]

We question whether there needs to be some form of quality assurance to ensure that the risk classification of medical devices, as stated by the device’s manufacturer, is indeed correct and represents the actual use of the device in the community.
Proposal B: Publication of medical device regulatory decisions

Interview participants showed majority support for Proposal B (n=13/16), which aims to publish regulatory decisions for medical devices on the TGA website. As all of the participants were in favour of increasing the amount of information published about ARTG decisions online, we do not recommend the adoption of Option 1 or 3, as outlined in the RIS.

Advantages of Proposal B

The most commonly identified advantage of this proposal was its ability to increase the transparency of TGA regulatory processes and decision making. Participants noted difficulties in accessing information about devices listed on the ARTG, and welcomed any initiatives which would help improve the accessibility of this information and improve transparency of TGA processes. It was also noted, as a consideration, that increasing transparency in this manner may open the TGA to criticism over the quality of evidence considered in the decision making process, but that this should not detract from the additional benefits of improving transparency.

Participants indicated that there is a precedent from within the prescription medicine industry to expand the information presented on regulatory decisions, namely the successful Australian Public Assessment Reports for prescription medicines (AusPAR) initiative. An equivalent initiative, intended to broaden the information provided on registered medical devices, in the same vein as AusPARs would help inform both consumers and clinicians about the best-use for new medical devices, particularly those that are not yet established in practice. However, the ability of the new system to provide this benefit is contingent upon the type of information provided on devices, which at this stage appears to be unclear.

Limitations of Proposal B

The most commonly identified limitation of Proposal B highlighted by participants was the increase in resources required by the TGA, including time, money and staff. However, it does not seem unreasonable, as outlined in Option B, to absorb the cost of this new process through a cost-recovery system. Under this system, the additional cost of $215 for simple decisions and $1197 for complex decisions would be absorbed by manufacturers of medical devices applying for certification. The estimated fees outlined in the RIS were not available at the time of our interviews, so we cannot comment on the ability of industry to absorb this cost. However, it was largely acknowledged that regulatory mechanisms and processes should not stifle innovation and that medical devices that are valuable to patient care should be made available in a fast but safe manner.
Consumer advocates also indicated that the average consumer is unlikely to visit the ARTG website to access this additional information. However, it was noted that this information would be valuable to consumer advocates that act on behalf of consumers, and to employ knowledge translation strategies to make the information about decisions more accessible to consumers where deemed necessary.

**Which kinds of devices should decision making information be published for?**

Participants indicated a preference to have the additional information approved for all medical devices (n=7/16), however 5 participants had no response. As the majority of medical devices registered in Australia fall within low-risk categories, the estimated time and cost to provide this information would be minimal. In regards to emerging breast imaging devices, such a low-cost initiative would highlight to consumer advocacy bodies and clinicians, that there is little evidence of efficacy or effectiveness considered during the certification process for these devices – a fact that is found to be surprising by the vast majority of the participants. Elucidating the lack of evidence considered during the certification process for these devices will help inform consumers and clinicians when deciding whether to use or recommend one of these devices, either as an adjunct or in lieu of regular breast screening procedures.

**Publication of regulatory decisions for devices that are rejected**

Participants shared nearly unanimous support for the publication of decisions on devices for which market approval was denied (n=15/16). The most commonly noted benefit of this Proposal was to provide justification for why certain devices that are available internationally are not also available in Australia. This information would be valuable for clinicians and consumer advocacy groups that are regularly faced with queries about devices that are not available in this country. Furthermore, this Proposal would increase the transparency of the TGA’s decision making process, which would have the added benefit of highlighting quality control issues in companies that are repeatedly rejected for certification. Participants also noted that identifying these issues may also be useful for regulatory bodies in neighbouring countries, such as New Zealand.

As with the previous proposal to publish regulatory decisions for devices that receive certification, participants also indicated that publishing rejected applications on the TGA website would require increased resources. However, as the cost of these rejected outcomes has been accounted for in the costing for Option 2, we refer to our previous comments on pages 4-5 in regards to the financial cost of this proposal on industry. Similarly, it was noted that regular consumers are unlikely to access the information presented on the ARTG website, however, this
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information would be useful for clinicians and consumer advocacy groups that use this information to inform consumers about devices. Finally, participants considered that increasing the transparency of device rejections may also allow companies that have been repeatedly rejected on reasonable grounds to publicly dispute these rejections through various media platforms, increasing time and resources needed.

Recommendation for Proposal B

Based on the responses of participants in our community consultation, we conclude that the most appropriate course of action for Proposal B is Option 2. The development of the AusPAR scheme has been largely praised since its inception, and a move towards a similar system for medical devices is welcomed. However, the benefit of this Proposal for emerging breast imaging devices depends on the type and amount of information published for each device. While there remain issues relating to the risk-classification of these devices, it would be valuable to both consumers and clinicians to understand the level and quality of evidence for safety and efficacy that was considered at certification for use in Australia. Therefore, we recommend that the information provided about medical devices include the evidence that was assessed to determine their utility for an intended purpose, and that this process should be applied retrospectively to devices that are already on the Australian market.

Proposal C: Abolition of requirement for TGA conformity assessment for Australian manufacturers of lower Class medical devices (including IVDs).

Like Proposal B, participants also shared majority in-principle support for Proposal C (n=11/16), which aims to remove conformity assessment requirements for Australian manufacturers of low-risk devices. However, unlike the previous proposal, participants’ support of this arrangement was contingent upon the ability of the TGA to clarify a range of extra conditions.

Conditions and limitations of Proposal C

Firstly, participants showed concern around the lack of Australian context in the conformity assessment process for devices, when certification is received from an international regulator. This issue is particularly relevant for emerging breast cancer imaging devices as they are classified as low risk (Class IIa) in Australia, yet still pose significant risks to consumers through false-positive and false-negative test results. There are a number of variables that can influence conformity
assessment procedures, including (but not limited to) variations in health system funding and structure, national mammographic breast screening programs, incidence of breast disease, population demographics, and socioeconomic status. Without an adequate consideration of these factors from an Australian context, the results and requirements for international conformity assessments may substantially differ from Australian standards.

Similarly, participants raised questions over the standards being used to certify international regulatory bodies offering third party conformity assessment for medical devices. A number of participants highlighted concerns with European Commission (CE) certification processes, particularly in the complementary medicines industry, and indicated that similar issues may also exist in the certification of medical devices. Comparatively, participants placed greater trust in the Food and Drug Administration’s (FDA) 510(k) process for certifying medical devices in the United States, however, it was suggested that any international regulator considered in this Proposal, including the FDA, should be required to pass rigorous quality assurance procedures before their conformity assessment rulings should be accepted for these imaging devices.

One participant also raised concerns over whether there is the potential for this Proposal to impede or diminish the value of Proposal B. Specifically, it was questioned how/if external conformity assessment procedures would affect the publication of decision making documents for medical devices (similar to the AusPARs), given that the conformity assessment would not be conducted by the TGA. Without clarification on these conditions and limitations, there was not majority support for this Proposal (n=7/16).

Advantages of Proposal C

Assuming that the above conditions are able to be adequately addressed, participants acknowledged several advantages of Proposal C. Firstly, this Proposal would require less duplication of regulatory processes, i.e. if a device has received adequate certification by the FDA it does not require detailed TGA conformity assessment, and therefore require fewer resources. As outlined in the RIS, this will potentially lead to significant cost savings for the TGA depending on the type and number of conformity assessments they receive each year. Additionally, the reduction in double-handling of regulatory procedures will improve the speed at which new medical devices and services will be made available to the community. An additional benefit of this proposal, as noted earlier, relates to differences between the risk-classification of emerging breast imaging devise between the TGA and the FDA. As the FDA categorises these devices in a higher-risk category than the TGA, it is
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possible that these devices may be required to pass a more rigorous assessment in order to receive conformity assessment.[20]

Recommendation for Proposal C

Based off of the responses from our participants, we recommended Option B as the most appropriate course of action to take for this proposal. The significant cost savings, coupled with the reduced time to market for new and innovative medical devices, give merit to this proposal. However, consumer advocates, researchers, and clinicians noted concerns around the manner in which external bodies would be certified to operate at Australian standards, as well as the lack of Australian context in regulatory decision making for devices which were not considered to be ‘low risk’, even though they are classified as such.

Final remarks

The TGA should be commended for their willingness to engage all sectors within the community during the reform consultations that have taken place over the past four years. We look forward to the opportunity to participate in future discussions around regulatory reform in Australia.

Sincerely,

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