MTAA Response to TGA Consultation "Proposed application audit framework for medical devices" – July 2023

Consultation proposal and question 1

Proposal

In this consultation, we are proposing to publish a set of risk factors that influence the likelihood that a medical device will be selected for non-mandatory audit. We propose to review and update the risk factors every two years, with additional ad-hoc reviews and updates should the need arise (e.g. if there is a critical safety signal). We will also report on trends and the types of devices selected for non-mandatory audit and the outcomes of those audits. The risk factors will be broadly categorised into the following 3 categories:

• risks relevant to the regulation and approval of the device

• risks relevant to the quality of the clinical evidence

• risks relevant to the sponsor, manufacturer, or type of device

Question

Is there any additional information that the TGA could publish about the new application audit framework that would help with improving the quality of applications to support more timely inclusion of devices?

MTAA Response

MTAA welcomes and supports this proposal of publishing the factors that influence the likelihood of an audit. As stated in the consultation paper, having risk factors gives sponsors an opportunity to have more transparency and predictability of approval timelines. Predictability of timelines is crucial for business planning including supply chain management which has become even more important in this post COVIS environment.

We do however consider that the 2 year frequency for update and publication is too long and a 12 month cycle would provide better information for sponsors.

Additional information to consider:

- When risk factors are published, it is important that the TGA provides the rationale to why these have been selected. Sponsors should have visibility to the information that TGA use to determine risk factors.

- When devices are selected for non-mandatory audit, TGA should provide detailed information outlining the reason for selection. This will not only help sponsors but allow TGA to use this to inform future risk factors.

- In relation to risks relevant to the regulation and approval of the device, TGA indicates that devices that are classified differently in Australia compared to other countries may be selected for a non-mandatory audit. This should not be a significant factor that should determine the need for a non-mandatory audit. This is especially true for lower and medium risk class devices. Regardless of the difference in classification across various jurisdictions, as

long the evidence of conformity supports the risk classification of the device in Australia, the application should not be subjected to any additional scrutiny.

- Within the consultation TGA lists a number of 'additional documents' that may be requested by exception based on identified risks and the reason the application was selected for an audit for medical devices – such as sterility validation, biocompatibility and viral inactivation reports. Currently, the type of documentation request for a Level 2 audit for medical device applications is limited to the provision of the device IFU, labels, Clinical Evaluation Report (including Magnetic Resonance Safety assessment report), and Risk Assessment documentation. Any changes to the current audit framework should not result in the request for additional documentation such as those listed in the consultation paper. This is not in alignment with the TGA's overall intention to simplify the current process while recognizing the assessments already undertaken as part of other overseas regulator approvals.

- Simple flow charts/visual aids/case studies and examples can be helpful for readers.

- There should be clear timelines for the statement in the consultation "We will also report on trends and the types of devices selected for non-mandatory audit and the outcomes of those audits."

- A pre-assessment criteria in the form of a checklist can be useful for sponsors to help determine whether the device will get selected for an audit.

- With regards to risks relating to sponsors and manufacturers, is this list going to be made public? If TGA has any concerns about certain Notified bodies, is this also going to be made publicly available?

Consultation proposal and question 2

Proposal

In this consultation, we are considering developing a proposal to Government to amend Regulation 5.3 to limit mandatory audits to the following types of medical devices, unless supported by TGA CA, EU MDR or EU IVDR certification:

• a medical device that is: a Class III medical device.

• an IVD medical device that is: o for self-testing for point of care testing o for managing or monitoring the treatment of infections diagnosed with a Class 4 IVD o an IVD where the TGA is not satisfied that appropriate conformity assessment evidence is held to demonstrate that product assessment has taken place o a Class 4 IVD o a Class 4 in-house IVD o an IVD companion diagnostic device that provides information that is essential for the safe and effective use of a corresponding medicine or biological.

Question

Are there any concerns with limiting mandatory audits to high-risk devices only, noting that the TGA may select any device for a non-mandatory audit if required?

MTAA response

No concerns with the proposal.

Can TGA provide further insight to this point: "an IVD where the TGA is not satisfied that appropriate conformity assessment evidence is held to demonstrate that product assessment has taken place". Sponsors experience that many IVDs are selected for audit, with this being the only point applicable, yet it is unclear what exactly TGA is looking for.

Furthermore for this point “an IVD where the TGA is not satisfied that appropriate conformity assessment evidence is held to demonstrate that product assessment has taken place” - a device that does not have satisfactory evidence of conformity should not pass TGA’s pre-liminary assessment and therefore the application would not progress to the next stage. As such there is no value in including these devices within the scope of Regulation 5.3 for mandatory audits.

Consultation proposal and question 3

Proposal

In this consultation, we are proposing amendments to Regulation 5.3 to remove the mandatory audit requirement for all medical devices (including IVDs) supported by US FDA PMA certification.

Question

Are there any concerns with not subjecting high risk medical devices (including IVDs) supported by US FDA PMA certification to mandatory audits, noting that the TGA could select any such device for a non-mandatory audit if required?

MTAA response

No concerns with the proposal. MTAA welcomes this amendment and believes that this will have a positive impact and increase access of devices and medical technologies to the Australian patients.

Question for TGA – will this proposal also include devices that are considered "specified medical devices" – i.e. those that contain medicines or materials of animal, microbial, recombinant or human origin?

A couple of recommendations for TGA's consideration

1. While we understand that in practice TGA does do it, we recommended that the acceptable comparable overseas evidence table (from the Therapeutic Goods (Medical Devices - Information that Must Accompany Application for Inclusion) Determination 2018) be updated to allow additional evidence for certain classes of devices. For example, allowing evidence that is accepted for higher risk devices to be used to support devices which happen to be of a lower risk classification, such as:
    - Class Is or Class IIa devices to utilise US FDA PMA approvals as evidence.
    - Devices which have a lower classification in Australia compared to Singapore and Canada, should be able to utilise the evidence from those countries. For example, a device which is Class IIa in Australia should be able to use a Class C or Class D Singapore Registration as evidence, rather than only a Class B Registration.
2. Consider removing mandatory audits for medical devices applications supported by Japan's Ministry of Health, Labour and Welfare (MHLW)/PMDA Pre Market Shonin Approval Certificates in recognition of the extensive level of regulatory review and assessment undertaken by PMDA.
3. Consider removing mandatory 'Technical File Review' audits for IVD applications supported by US FDA 510 (k) in recognition of the extensive assessment undertaken by FDA. TGA may instead limit the level of assessments a Level 1 audit.

Consultation proposal and question 4

Proposal

In this consultation, we are seeking feedback on whether it would be worthwhile establishing a pathway for Class III medical devices based on MDSAP certification and US FDA 510(k) approval.

Question

What are the merits or risks of establishing a pathway for Class III medical devices based on MDSAP certification and US FDA 510(k) approval?

MTAA response

We are very supportive of this pathway being established to allow greater access of devices to Australian patients and support TGA's efforts in this area of regulatory reliance. The merits in this case certainly outweigh the risks.

Merits

- Earlier access where sponsors are experiencing significant delays for EU approvals.
- Earlier access to those devices that are launched in the US before other jurisdictions.
- Earlier access to medical devices that have a risk classification difference in EU compared to AU. These devices would currently have to undergo a TGA CA which may deter some sponsors from bringing the device to the AU market.
- Cost effective compared to a TGA CA.

The risks are negligible as these applications are likely to be selected for an audit. MDSAP for QMS + CER, Risk Management Report, PIC, PIL, DFU, MRI (if applicable) for product assessment reviews seems a reasonable protection against any risks.

Finally, it is worth noting that many devices that would be Class IIa in Australia are only considered to be Class I, according to the US FDA. As such, many of the instrumentation devices that are required for the class III implants are US-FDA 510(k) exempt. Even if a Class III pathway is created as an option for US-FDA 510(k) products, we will still need a pathway for the registration of the associated instrumentation. Therefore, the TGA should also consider creating a pathway for Class IIa devices in Australia that are considered to be US-FDA 510(k) exempt. Currently, the only available option for these class IIa instruments that are not planned for release in Europe is through TGA conformity assessment (if they are not registered in Japan, Canada, or Singapore). This could be achieved through an exception list of instrumentation where the medical device classification differs.

Consultation proposal and question 5

Proposal

In this consultation, we are proposing to formalise the requirement for the submission of the IFU and CER for all Class III devices supported by EU MDR certification, and the submission of IFU, clinical and analytical performance evaluation reports for Class 4 IVDs supported by EU IVDR certification.

Question

Are there any concerns with formalising the requirement for the submission of: (a) IFU and CER for all Class III devices supported by EU MDR certification? (b) IFU and Performance evaluation (clinical and analytical) reports for all Class 4 IVDs supported by EU IVDR certification?

MTAA response

While it does not seem onerous to provide the CER for class III applications, there are some concerns with this proposal and MTAA does not support formalising the requirement of the submission of the CER.

MTAA does not agree that the CER should be important in information TGA's risk assessment for the following reasons:

- The information collected in the application form, together with the conformity assessment evidence (e.g. EU MDR or IVDR CE certificates), should be enough to make a decision on whether to select the applications for auditing. This information should cover the risk factors that mentioned in question 1 such as type of device, post market signals for that type of device, manufacturer, sponsor, regulatory reforms, and regulatory intelligence.
- If the CER is being requested to ensure confirmation that it exists and meets regulatory requirements, the DoC should be evidence enough.
- The fact the manufacturer has an EU MDR certificate should be evidence enough that the CER is thorough and meets the regulatory requirements given the additional scrutiny that MDR places on device approvals. This includes the effort that it takes to designate a Notified Body and the rigorous training that their assessors are required to complete.
- There seems to be duplication of work that has already been conducted by the Notified Body under MDR scrutiny as per the above point.

As per the consultation, TGA has been routinely asking for the CERs for applications supported by EU MDR certification. Sponsors have not found this to reduce their likelihood of being selected for a non-mandatory audit, in fact, there have been numerous cases where the TGA has not been able to assess the CER in the 20 working days and the application had been selected. Given this, we are concerned that routine submission of IFU and CER as attachments to ARTG applications is likely to result in more applications being selected for auditing, rather than less e.g., if the Delegate is unable to review the IFU and CER within 20 working days, this could result in the application being selected for non-mandatory auditing just so the Delegate can finish reviewing these additional attachments. Furthermore, with the current backlog of clinical assessments, MTAA is not confident that this CER review can be completed within 20 days.

The consultation also states that analysis has indicated 39% of applications supported by EUMDR certification were selected for audit, however further analysis has suggested that there is a

downward trend. This seems to suggest that the clinical evidence provided for the 39% selected was deemed satisfactory. This further supports the rationale for not providing the CER upfront and basing the non-mandatory audit selection on the other risk factors outlined in question 1.

Another suggestion is for TGA to focus on the post market surveillance of these devices with a lighter touch on the premarket (i.e., not providing CERs upfront) to see if there are any emerging issues.

Consultation proposal and question 6

Proposal

We will limit the number of substantial review rounds to two, with any additional (substantial) rounds to be by exception only.

Question

Do you have feedback about further measures to improve assessment timeframes?

MTAA response

MTAA would like further clarification for this question. The way this is proposed, it would mean there would only be one request for information during an application audit, before an application is potentially rejected. In other words; review round #1, followed by one request for information, followed by review round #2, before a decision is then made. A point of clarification is that technical documentation submitted to TGA are those that have already been reviewed and accepted by other comparable overseas regulators such as the European Notified Bodies, FDA. The initial request for any technical documentation (either in the form of a Level 2 audit for medical devices or a Technical File Review for IVDs) that would be considered to be within the scope of the audit should be in the form of an S41FH request and not considered to be 'Round 1" of "substantial review round" of questions.

If this is the case, the following points need to be taken into consideration:

- Limiting TGA requests for information to 'must-have' information, rather than 'nice-to-have' information.
- Educating TGA evaluators so that they do not waste time, and the number of review rounds, requesting information from the manufacturer to fill gaps in their knowledge of the medical technology.
- Questions need to be complete and clear.
- There needs to be an opportunity to seek clarification from the reviewer without this being considered a round via email or phone. In addition, it should be made clear that any minor clarifications sought are not considered part of a "substantial round".
- The second round of questions should not raise any new questions by the assessor.
- Implementing additional pre-submission engagement avenues to ensure both the sponsors and TGA have a good starting knowledge of the upcoming submission.

MTAA believes there is still some additional consultation required before this can be put in place especially for new sponsors. Also, component queues can vary with TGA and restricting the round of reviews after a single request for information does not address the issue of TGA resourcing and expertise which may still lead to long approval times.

If this was to be implemented, the applicant should be given more than the standard 20 work days to provide their response to the single request for information. Only providing 20 work days (or the minimum of 10 work days) is likely to result in more applications being rejected, and therefore more initial decisions being appealed under Section 60.

A suggestion to improve timeframes is for mandatory audits, selecting a greater proportion of application audits for Level 1 audit, as opposed to them all being Level 2. Having a system (based

on known risk factors) which results in 50% of mandatory audits being Level 1, and 50% being Level 2, could be a good target. This would reduce the amount of application audits that require a clinical review, which is the current primary cause for evaluation bottle-necks and lengthy assessment times.

Further clarification is sought on:

- Additional rounds will be by exception only.
- “Substantial review” or “substantial rounds” as there is currently no definition of this.
- Impact of ACMD review

Consultation proposal and question 7

Proposal

In this consultation, we are seeking your feedback on what information would be useful for sponsors to obtain greater visibility of application timeframes.

Question

What information could the TGA provide that would be useful for sponsors to have greater visibility of application timeframes?

MTAA response

This response should contribute to the digital transformation project and we look forward to contributing to this.

When an application is first selected for auditing, the TGA should inform the applicant of:

- Notification whether the application has been selected for a non-mandatory audit.
- The expected date to receive the one and only additional request for information (i.e., time to end of first review round).
- An estimated decision date based on current timelines and volume of applications on hand, assuming one request for information during the audit.
- Whether the application is expected to be referred to the ACMD for advice, and if so, which ACMD meeting it is likely to be considered at.

This would be more consistent with the approach taken for the TGA's medicines evaluation process, where milestone dates are provided to the applicant and updated throughout the assessment process.

Following this, an online portal should exist where sponsors can:

- Check the status of all their applications (new, variations) and where it is in the queue and with which component section e.g., under "evaluation/review", "waiting for an evaluator to be assigned" .
- Approximate days to completion.
- Decision pending – approximate days to decision.

This is crucial for sponsors to help their commercial teams for business planning and managing supply chains. A dashboard with real time data and statistics regarding how many applications are in the queue and current queue times would also be beneficial for sponsors.

General comments

1. MTAA welcomes the changes proposed in question 3 and 4 and look forward to working with TGA to establish how these can be implemented considering the conformance to clinical requirements may be demonstrated to FDA in a variety of forms including a manufacturer's commitment to post market results.

2. Currently the application audit letters sent to sponsors come from a template and sometimes documents that are not applicable/relevant for the device are requested (e.g., a request for PIC/PIL for a non-implantable device). We hope that this template is updated and more fit for purpose.

3. We suggest given certain risk factors are lower with MDR approved devices, there can be a greater focus on post market review and process with a lighter touch on the premarket assessment.

4. We suggest that with this new process timeframes are tracked and there be some visibility and reporting back to sponsors on this to ensure the new process is efficient.

5. As we have recommended CERs not be provided upfront and be used for risk factors, it should be removed form the risk factors.