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

September 2023

The members of Pathology Technology Australia (PTA) welcome the opportunity to comment on the TGA's Consultation "Proposed application audit framework for medical devices" and are supportive of TGA's publication of this consultation to provide more clarity for sponsors on the risks and requirements for selecting applications for Audit including, non-mandatory audits.

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?

PTA response

As many of our businesses are developing products with greater integration with technology and more innovative products, sponsors have greater need to understand the risk factors that form the criteria for mandatory and non-mandatory audits. This also remains true for sponsors of more "traditional" IVD products. The impact of the pandemic on approval timelines has significantly [redacted]ket timelines, with a ripple effect of lack of accessibility to Australian patients. To provide more informed and accurate timelines to businesses and Australian customers, more predictability in approval timelines is much needed.

Due to the current rate of innovation, continual strengthening, and global harmonisation of regulations in many major jurisdictions where products are manufactured and approved, PTA would respectfully request a shorter timeframe for review of these risk factors. We would therefore suggest an annual review in conjunction with the proposed ad-hoc reviews if necessary.

- Based on the published risks, decision tree/process flow charts can be useful to help sponsors to understand the potential for audit/ mandatory or non-mandatory.
- As per comment above- this would also apply to changes to a Class 4 IVD - the use of IVDR is still very new to many Australian sponsors, so clarity is sought on changes considered significant under IVDR and the potential of mandatory versus non mandatory audits as a consequence of these changes.
    - Note: in the consultation paper – some risks still appear to need further clarification for validity, e.g. why would a device with multiple comparable approvals still be at risk of a non-mandatory audit? This still reduces the predictability of approval times for sponsors and the rational is unclear.
- While the Application Audit (technical files review) of IVD medical device application version 1.1 is very useful to determine the requirements for a an IVD application audit, further enhancement is needed, for example a Checklist or clear TOC to guide sponsors on requirements for both mandatory and non-mandatory audits.
- A clear indication of what the TGA considers not to be current clinical evidence. It could be communicated in the context of assuming all other risk factors are not an issue. This would be useful to Sponsors when determining whether or not to submit an inclusion application, whilst adding efficiency to the TGA process because Sponsors would not submit applications with ‘old’ clinical evidence.
- When selected for non-mandatory audit, the TGA provides reasons to the Sponsor for the selection and a mechanism established for a Sponsor to challenge the selection decision. This will educate Sponsors for future [redacted]ing efficiencies over time, and ensure consistency and [redacted]e selection process.

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:
  - for self-testing for point of care testing
  - for managing or monitoring the treatment of infections diagnosed with a Class 4 IVD
  - an IVD where the TGA is not satisfied that appropriate conformity assessment evidence is held to demonstrate that product assessment has taken place.
  - a Class 4 IVD o a Class 4 in-house IVD
  - 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?

PTA response

PTA are aligned with and support TGA's proposal to limiting audits to high-risk devices, this will allow TGA to focus on products are considered of greater safety concern.

We recommend removal of the superfluous statement - "an IVD where the TGA is not satisfied that appropriate conformity assessment evidence is held to demonstrate that product assessment has taken place" from the scope of Regulation 5.3.

Due to the specificity of the comparable overseas regulator's determination [redacted] certain levels of evidence towards conformity assessment [redacted] tated as requiring mandatory application audit e.g., MDSAP plus 510k. As such, there is no value in including these devices within the scope of Regulation 5.3 for mandatory audits.

Refs:
Therapeutic Goods (Overseas Regulators) Determination 2018- external site
Therapeutic Goods (Medical Devices—Information that Must Accompany Application for Inclusion) Determination 2018.

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?

PTA response
PTA are aligned with and support TGA's proposal to remove mandatory audits for all IVDs that are supported by FDA PMA.

PTA understands that TGA are still building experience and confidence in the use of FDA PMA and there may be a higher rate of selection of applications for non-mandatory audits. While this is understandable sponsors will still be in a position of having very little idea of how long this assessment will take. There are no statutory timeframes associated with mandatory or non-mandatory audits and it will continue to be difficult to provide any level of predictability to business and customers. While it is noted that the quality of the data submitted dictates the assessment time, and assuming Figure 3 is to be used as the standard process, sponsors would request an indicative timeframe to be provided at time points when requests for updates are submitted. This is particularly of importance at the component assessment queue- which is subject to varying timeframes.

Of additional concern – is the requirement to provide the CER and its [redacted] approval times. To reduce the risk of non-mandatory audit this consultation indicates the CER must be current. There is a potential for the CER to be older than required when "picked up" for review. With no visibility on approval timelines, there will be opportunity to the sponsors to flag

a proactive update request to the manufacturers. This extended review time could be the only reason to "trigger" a non-mandatory 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?

PTA response
Not applicable to IVD's, no comment from PTA.

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?

PTA response
PTA would like to understand the exact rationale for the provision of PE reports for Class 4 IVDs supported by EU IVDR certification. EU IVDR certification is evidence of appropriate scientific validity and clinical and analytical performance. The submission the clinical and analytical performance reports at the initial application stage increases the TGA's [redacted]fficiencies to the process, only to verify a decision already made by a comparable overseas regulator. There can sometimes be numerous analytical performance reports, increasing the likelihood of the TGA not completing the review within 20 working days of initial application

submission, hence leading to selection of the application for non-mandatory audit.

PTA proposes for a Class 4 IVD application with has IVDR approval, be supported by the PEAR and TDAR reports only. These reports confirm the clinical evidence, based on data on scientific validity, analytical performance and clinical performance of the device has been verified and deemed compliant with the IVD Regulation and that the manufacturer holds the supporting documentation for the device. They have been issued by a Notified Body and should provide sufficient information to inform the TGA as to whether the device meets the Australian regulatory requirements. If these reports are not deemed sufficient, the TGA could then select the application for a non-mandatory audit.

PTA is aware of MTAA's position on less focus on the premarket assessment of the EU MDR approved product and instead focus on the post market surveillance – PTA are also aligned with this approach for IVDR approved products.

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?

PTA response
This proposal has caused multiple concerns to members due to this significant deviation from current practice. While in theory, this approach makes sense to reduce the volume of time spent assessing submissions, with multiple back and forth information requests, more clarification is required to completely understand what is considered a request for information. For example, when an initial application is submitted, TGA then send a request for an information under s41FH. Is this initial request factored in as one of the substantial reviews?

[redacted]

As discussed in the previous regulatory and technical forums with TGA, many sponsors are in favour of more consolidated requests for information. However, if these consolidated requests are significant in size this could have

the potential for sponsors and manufacturers to need more time, than the current mandatory 20 working days to provide the additional information. Also discussed at these forums, some questions asked by reviewers may need additional clarification as their purpose is not always clear in the formal request for information. The criteria and ability for clarification on the formal request for information would need to be defined and not considered a second substantial review. For example, could a sponsor seek clarification from the reviewer via email or phone, making it clear this was not considered a "substantial round"

In addition, for complex or more innovative products, it can be more beneficial and appropriate for the manufacturers R&D team or scientific team to have a meeting with TGA during the review process, to discuss the technical details pertaining to the benefits and risks of certain products. In certain cases, this has previously been accepted as supplemental support for the clarification of the technical aspects of the products. Would meetings like this still be considered acceptable within the realm of one substantial review or considered a separate review thus impacting on the number of allowed reviews?

PTA would also like to note that the quality of the TGA's reviewer's questions have an impact on the number of substantial review rounds and additional communication required with the TGA. Is there a process for TGA' reviewers be assessed, audited and measured to ensure the quality of their questions don't impact the number of substantial review rounds an application requires?

PTA is not completely averse to this proposal, to try to benefit from the efficiencies that could be gained from these consolidated requests, however we believe more discussions between Industry and TGA are necessary, to clearly establish guardrails and understanding of this proposal.

<u>Consultation proposal and question 7</u>
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
[redacted]**ould the TGA provide that would be useful for sponsors to have greater visibility of application timeframes?**

PTA response

PTA are confident that the upcoming Digital transformation project should alleviate many of the IT challenges that sponsors have in the visibility of their submission status.

However, since this project is yet to officially commence, it is likely to be some time before the impact of the transformation is seen by sponsors.
For current application timeframes it would be useful to know once the submission has been submitted to TGA;

- TGA's acknowledgment of the application and its position in the "queue' with estimated number of days for initial review. Although there is a 20 working day requirement for TGA to review – this has not always been the experience of sponsors.
- When selected for audit and submitted by sponsors – again an update of the position in the 'queue' and an estimation of days for assessment to be completed would help sponsors and manufacturers to plan their market activities.
- When the audit has been ongoing for some time – if sponsors request a status update it would be helpful to get an actual timeframe. Current responses appear to be autogenerated and gives no indication of exactly what part of the process (as per Figure 3) that the submission is at or if a reviewer has even been assigned.
- An indication of ACMD review and the timeframes associated with the next review and potential publication of outcomes. This would be particularly helpful for planning purposes and if medical or R&D support would be required from the manufacturer.

PTA recognises all the work the TGA have contributed to this consultation and are appreciative of the opportunity to provide feedback and comments on behalf of the IVD Industry.

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