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Boston Scientific feedback to TGA proposed application audit framework for medical devices.

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1 INTRODUCTION

On 24th July 2023, the TGA opened the consultation: *Proposed application audit framework for medical devices*, which sought feedback on how TGA select medical device applications for audit and how they conduct those audits.

As per TGA, feedback was sought on: "the key elements of the proposed audit framework:

- risk factors informing non-mandatory audit selection
- criteria for mandatory audits
- the evidence to be provided with applications to inform audit selection
- limiting the number of substantial assessment rounds
- mechanisms to improve visibility of application audit timeframes
- cost recovery measures for non-mandatory audits.
- pathways for Class III devices with US FDA 510(k) approval."

Boston Scientific (BSC) recognise TGA's intent to minimise regulatory burden, cost, and impact on the medical devices industry and the healthcare system by streamlining the current audit framework while maintaining a risk-based approach.

BSC support TGA's proposal to streamline the way they conduct audits under an updated framework and welcome the opportunity to provide comments on the TGA *Proposed application audit framework for medical devices* consultation.

2 BOSTON SCIENTIFIC RESPONSES TO TGA QUESTIONS

Question 1 - 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?

Answer 1:

Applications for medical device inclusions into the ARTG are made based on requirements per regulations. Clearly defining the risk factors that influence TGA's decision to select an application for non-mandatory audit are therefore believed to contribute to higher quality of applications.

TGA's proposal of risk factors make up a practical guide, however, it is still too general and presents opportunities for improvement to increase clarity and facilitate higher quality of applications. The following are recommendations for improvement:

- TGA should officially define 'well-established technology' and its criteria.
- TGA should define clear timelines and frequency for reporting on trends and the types of devices selected for non-mandatory audit and the outcomes of those audits.
- TGA should define 'currency' for literature review, post market, and clinical evidence reports (CER), separately.

Question 2 - 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?

Answer 2:

No. However, BSC believe TGA's proposal to government should seek 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, **or FDA PMA**. This in alignment with the third element of the proposed application audit framework.

Question 3 - 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?

Answer 3:

No.

Question 4 - 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?

Answer 4:

Merits:

- Favours market entry and promotes patient access to new technologies.
- Supports Regulatory Reliance and allows the efficient use of resources by industry, healthcare, and ultimately, serves Australian patients by facilitating earlier access to medical devices.

Risks:

- US FDA 510(k) applications and approvals are based on being able to demonstrate substantial equivalence to an already marketed device. Per the Australian Therapeutic Goods (Medical Device) Regulations 2002- Regulation 3.11, clinical evaluation procedures must be applied to the device, for the purpose of demonstrating that the device complies with the applicable provisions of the essential principles. Where in contrast, the US FDA 510(k) application process does not require a clinical evaluation report. Consideration must be given to the impact of differences in requirements (such as these and others).
  Further, there may be instances where the device which the 510(k) claimed equivalence to is not marketed in Australia. This should not prevent manufacturers from being able to leverage the 510(k) approval.

Question 5 - 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?

Answer 5a:

The amendment of Regulation 5.3 resulted in applications supported by certification under the EU MDR, no longer being subject to mandatory application audits. Therefore, the provision of the IFU and CER documents should not be required unless requested as part of a non-mandatory audit.

BSC would welcome TGA providing industry more context to this request and how the IFU and CER would be utilised for those applications which do not require a mandatory audit.

It is BSC position, creating a new requirement to provide the IFU and CER with all class III applications supported by EU MDR will be detrimental to the original intent of the amendment of Regulation 5.3 and will result in increased review timelines for applications that do not warrant a mandatory audit.

Should TGA decide to implement this new requirement despite the potential risk to timely access to new technology, BSC strongly recommends that:

- Exemptions are allowed for:
    - New class III applications resulting from the change in legal manufacturer
    - New class III applications for 'well-established' technologies. If implemented, this requirement should be limited to novel high-risk class III devices.
- When available, manufacturers should be able to provide the CEAR instead of the CER in order to facilitate an expedited review by TGA
- TGA publishes a detailed assessment criteria (E.g., checklist) of what they are looking for during the initial application triage phase, before deciding whether an application is selected for a non-mandatory audit.
- The pre-assessment timeframe of 20 working days should not be impacted
- System should be updated to support larger files as IFU/CER will be larger than standard attachments

(b) IFU and Performance evaluation (clinical and analytical) reports for all Class 4 IVDs supported by EU IVDR certification?

Answer 5b:

BSC do not commercialise IVD medical devices.

Question 6 - Do you have feedback about further measures to improve assessment timeframes?

Answer 6:

It is BSC position the root cause for extended assessment timeframes is multi-faceted and not only attributed to insufficient evidence to substantiate compliance. Therefore, limiting the number of substantial assessment rounds to two rounds of review may not address the long assessment timeframes the industry is experiencing.

BSC would like to make the following recommendations for how quality of applications and assessment timelines could be improved:

- TGA should implement additional pre-submission engagement avenues to facilitate TGA's product understanding and manufacturers' understanding of what the assessment is going to involve. TGA has recently shifted to minimise contact with sponsors which has only been detrimental to their review timelines.
  Although TGA state there are pre-submission meetings avenues, requests both at pre-submission and during assessment are often declined.
- TGA should remove manufacturers' evidence (ME) upload and approval prior to application. The ME should be included as part of the device application and TGA should review during the 20-business day decision period.
- TGA should issue official 'well-established' technology definition and criteria. TGA should also provide a detailed list of examples.
- TGA should limit the request for IFU and CER/CEAR to novel class III technologies only
- Whilst we are in alignment with the consolidation of component assessments to avoid duplication in questions issued, there is concern this approach may result in longer review timelines. If there is a backlog in one TGA section such as clinical review or sterilisation (as has been the experience in recent years), the first round s41JA request will be delayed waiting for consolidation and may be issued much later in the review process.
- To address the above, TGA should consider defining and legislating target assessment timeframes, similar to legislated conformity assessment timelines, E.g., First *substantial*

review round issued within 20 working days and second round within the following 3-4 months. This will prevent applications to receive first substantial review round several months post initial submission.

- TGA should ensure questions from all component assessments are not only consolidated as part of the new substantial review round, but also considered for any follow-up questions. The second round should be issued only if there are gaps from the response to the first round, it should not be a new set of questions.
- TGA should define criteria for providing exceptions to allow for additional rounds of question
- TGA should review suitability of the 20-working day timeframe manufactures have to respond to questions, given questions will be consolidated from all assessment components.

Question 7 - What information could the TGA provide that would be useful for sponsors to have greater visibility of application timeframes?

Answer 7:

1. TGA's eBusiness portal should be able to show the following:

- What assessment components will be required for any given application? Pre-assessment, clinical, engineering, risk management, labelling, ACMD, final admin (TGA) to do the audit report (first or second final review) etc.
- If an application is currently under review and by which component team, or if it is still in queue
- How many applications are in queue, especially in front of the subject application.
    - Alternatively, an expected time before the application is picked up for review for each assessment component
- Status of the applications – assessment in progress, assessment completed etc.
- Expected processing time for each component assessment for any given application sitting with TGA (not just on average processing times)

2. TGA should also clearly communicate risk of applications being referred to ACMD.
3. The system should have the capability to send out automatic communications with status updates for each application sponsors have with TGA.
4. TGA will need to modify the way they currently collaborate with industry by creating new communication channels and actively engage with industry throughout the application review process.

The above will also reduce the number of sponsors or times sponsors reach out to TGA following up on status of their applications and will TGA more time back to review.

Given the digital transformation project is a long-term initiative, alternatives should be sought to address the gaps outlined above.

BSC would like to thank the TGA for engaging with industry in this matter and are looking forward to actively collaborating towards a streamlined audit framework that builds on regulatory reliance and continues to ensure the highest quality of medical devices in Australia.