Australian Government
Department of Health and Aged Care
Therapeutic Goods Administration

Proposed application audit framework for medical devices

Version 2.0, July 2023

TGA Health Safety Regulation

Contents

Executive summary

The Therapeutic Goods Administration (TGA) is responsible for regulating the import, export, and supply of medical devices, including in vitro diagnostic (IVD) medical devices in Australia.

Before they can lawfully supply most medical devices in Australia, sponsors must apply to the TGA to include the product in the Australian Register of Therapeutic Goods (ARTG).

The TGA assesses the medical device application against the regulatory requirements specified in the *Therapeutic Goods Act 1989* and the *Therapeutic Goods (Medical Devices) Regulations 2002* (the Regulations). Some applications are audited, which is a more thorough assessment.

We are reviewing our framework for how we select applications for audit and how we conduct audits across all device classifications. This is in response to:

- changes to the European Union (EU) regulations for medical devices and IVDs, including enhanced standards, processes, and clinical evaluation requirements
- the amendment of Regulation 5.3 in July 2021 to excuse applications supported by certificates under the new EU regulations from mandatory audit
- concerns raised by industry about existing processes, timeframes, and predictability
- a need to flexibly target our premarket assessment resources to areas of risk.

The framework needs to allow regulatory effort to be aligned with risk and streamlined. This will reduce regulatory burden and cost and provide the healthcare system with timely access to new technologies that have been shown to be safe and effective.

This consultation is seeking feedback on the key elements of the proposed application 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.

We also seek feedback about pathways for Class III devices with US FDA 510(k) approval.

Recent regulatory changes

The EU recently introduced a new legislative framework to ensure more robust and transparent regulation of medical devices, including IVD devices. Most medical devices in Australia (above Class I) are supported by EU certification and are

transitioning to the new EU Medical Devices Regulation (MDR) that started in May 2021 and with staggered end dates between May 2026 and December 2028.

The EU IVD Regulation (IVDR) started on 26 May 2022, with transition periods staggered to end between 26 May 2025 and 26 May 2027. IVD manufacturers with EU certification need to transition to the EU IVDR or seek alternative certification.

To recognise the significantly enhanced standards, processes, and clinical evaluation requirements in the new EU Regulations, the Australian Government made changes to Australia's medical device regulatory framework in July 2021, to repeal Regulation 4.1 and amend Regulation 5.3.

The repeal of Regulation 4.1 changed the requirements for Class 4 IVD medical devices and medical devices that contain medicines or materials of animal, microbial, recombinant, or human origin. These medical devices no longer require TGA conformity assessment certification. Sponsors can now provide certification under the new EU MDR or IVDR to support an application for inclusion in the ARTG.

The amendment of Regulation 5.3 means that applications for any class of device supported by certification under the new EU MDR or IVDR, are no longer subject to mandatory application audits. However, these applications may be selected for a non-mandatory audit. This allows the TGA to review compliance with Australian-specific regulatory requirements, while also recognising the enhanced standards in the new EU Regulations. There are no audit fees for non-mandatory audits.

Regulation 5.3 still specifies that non-EU MDR applications for Class III and certain Class IIb medical devices must be selected for audit. Regulation 5.3 also still specifies that non-EU IVDR applications for Class 4 and certain higher risk IVD medical devices must be selected for audit. For these mandatory audits, sponsors must pay an audit fee prescribed in Regulation.

Current application audit process

Audit pathways

The TGA audits applications to verify that devices submitted for inclusion meet the relevant requirements. For some applications, an audit is mandatory under the legislation. All other applications may be selected for non-mandatory audit at the discretion of the TGA.

Table 1 outlines the type and class of device, and manufacturer evidence used, that determines if an application for inclusion in the ARTG must be selected for a mandatory audit under the legislation.

Table 1: Current audit requirements based on device class, type, and evidence

Class of device	Manufacturer Evidence	Mandatory audit?	May have non-mandatory audit?
Class I non-sterile, non-measuring	Declaration of conformity[1]	✗	✓
Class Is or Im	TGA CAC[2] EU MDD/AIMDD[3] EU MDR[4] MDSAP[5]	✗	✓
Class IIa or IIb not in Reg 5.3	TGA CAC[2] EU MDD/AIMDD[3] EU MDR[4] Japan MHLW/PMDA[6] Health Canada[7] US FDA[8] HSA Singapore[9]	✗	✓
Non-IVD devices in Reg 5.3	TGA CAC[2] EU MDR[4]	✗	✓
	EU MDD/AIMDD[3] Japan MHLW/PMDA[6] Health Canada[7] US FDA[8] HSA Singapore[9]	✓	N/A
Class III specified medical devices[10]	TGA CAC[2] EU MDR[4]	✗	✓
	EU MDD/AIMDD[3]	✓	N/A

[1] Declaration of conformity - under the Therapeutic Goods (Medical Devices) Regulations 2002
[2] TGA CAC - TGA conformity assessment certificate
[3] EU MDD/AIMDD - EC Certificate under Council Directive 93/42/EEC or Council Directive 90/385/EEC
[4] EU MDR - Certificates issued under Regulation (EU) 2017/745 on medical devices
[5] MDSAP - Certificates issued under the medical device single audit program (MDSAP)
[6] Japan MHLW/PMDA - Premarket approvals from Japan
[7] Health Canada - Certificate or licence under the Canadian Medical Devices Regulations (SOR/98-282)
[8] US FDA – United States Food and Drug Administration (US FDA) s513/s510(k)/PMA approval
[9] HSA Singapore – Health Sciences Authority of Singapore medical device registration
[10] Specified medical devices - other than IVDs, that contain a medicinal substance or materials of animal, microbial or recombinant origin intended for use in the body

Class of device	Manufacturer Evidence	Mandatory audit?	May have non-mandatory audit?
Class 1 IVD not in Reg 5.3	Declaration of conformity[1]	✗	✓
Class 2 or 3 IVD not in Reg 5.3	TGA CAC[2] EU IVDR[11]	✗	✓
	MDSAP[5] (+ product review) Health Canada[7] US FDA[8] HSA Singapore[9] EU IVDD[12] ISO 13485[13] (+ product review)	✗	✓
Class 4 IVD	TGA CAC[2] EU IVDR[11]	✗	✓
	EU IVDD[12]	✓	N/A
Class 1-3 IVD in Reg 5.3	TGA CAC[2] EU IVDR[11]	✗	✓
	MDSAP[5] Health Canada[7] US FDA[8] HSA Singapore[9] EU IVDD[12] ISO 13485[13]	✓	N/A

Current application review process

All ARTG inclusion applications must first pass preliminary assessment and those that do not must be refused. After passing preliminary assessment, depending on the class and type of device, and the manufacturer evidence used (described in Table 1), an application may be:

[11] EU IVDR - Certificates issued under Regulation (EU) 2017/746 on IVD medical devices
[12] EU IVDD - EC Certificate issued under Directive 98/79/EC on IVD medical devices
[13] ISO 13485 – ISO 13485 certificate from International Accreditation Forum conformity assessment body. The TGA stopped accepting ISO 13485 certificates for new Class 2 & 3 IVD applications from 26 May 2023

- approved without an audit
- undergo a mandatory audit
- undergo a non-mandatory audit.

The TGA has 20 days to triage the application and decide whether to select it for audit (Figure 1). During this period, the TGA may contact the sponsor to clarify matters or request additional information.

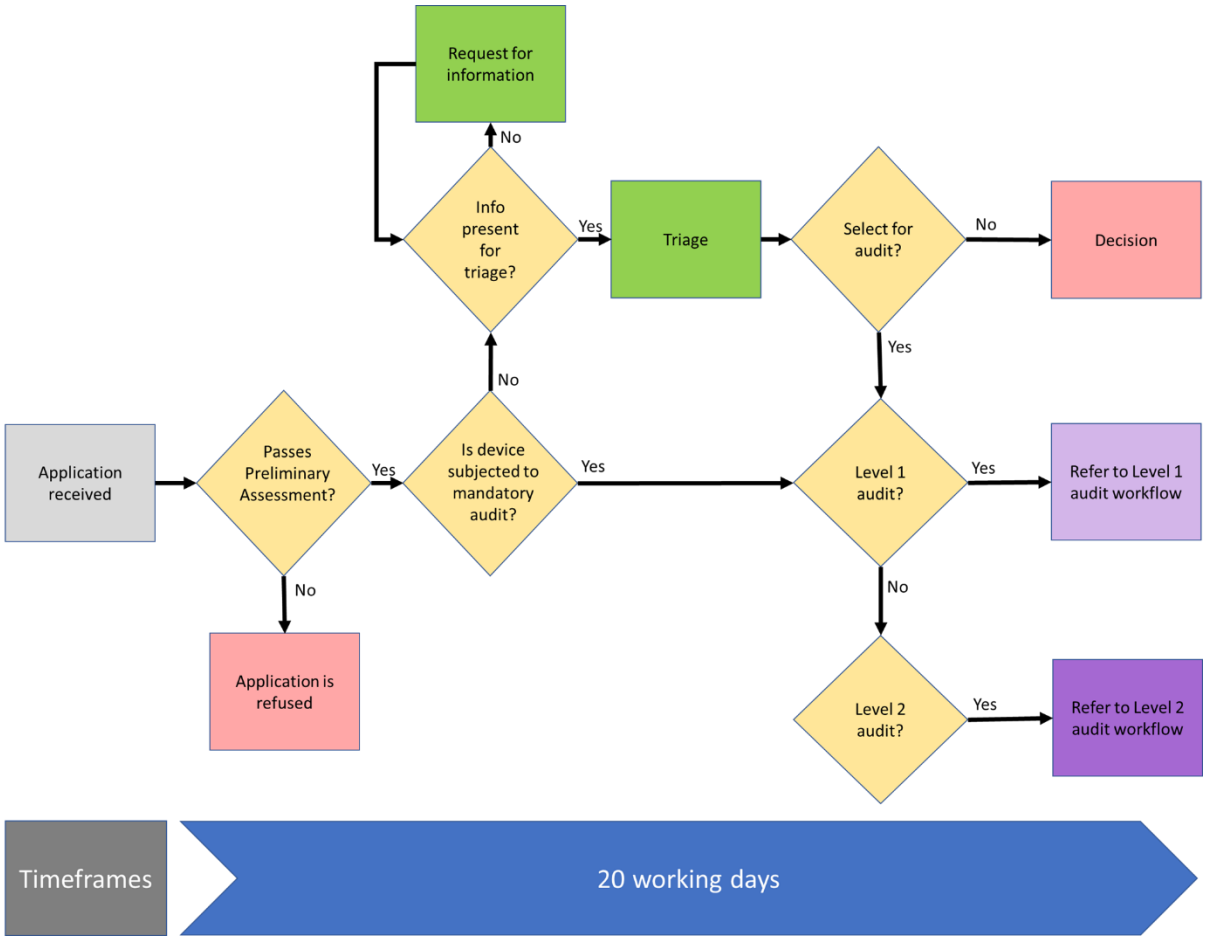


Figure 1: Application workflow – audit selection

Scope of audit

The TGA targets application audits (mandatory and non-mandatory) to identified areas of risk or concern associated with the technology type, the performance or use of the device, or to address evidence gaps in the application. Non-IVD mandatory application audits are either ‘Level 1’ (Figure 2), or ‘Level 2’ (Figure 3) and the assessment fee depends on the audit Level and the class of the device.

Level 1 audits

Level 1 application audits verify the sponsor’s application and evidence of conformity. Sponsors are typically required to submit (see Figure 2):

- the manufacturer’s declaration of conformity
- evidence of compliance with applicable system or procedure pack requirements

- evidence of compliance with certain standards (e.g., button battery safety or biocompatibility of materials for ventilators or positive airway pressure devices)
- copies of labelling, packaging, instructions for use, product manual, brochures, advertising material, patient implant cards and leaflets, and images of the device.

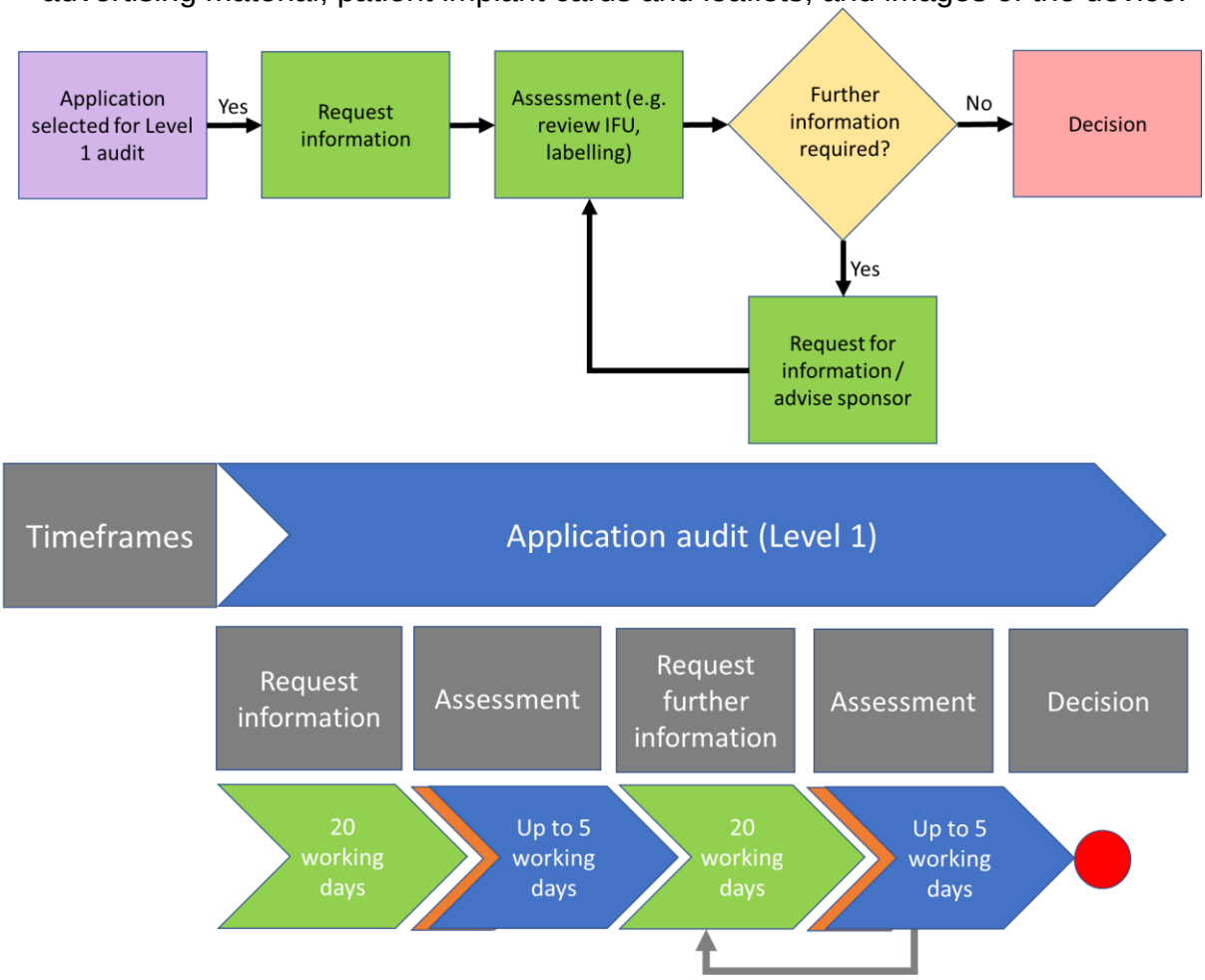


Figure 2: Level 1 application audit workflow

Level 2 audits

Level 2 audits target higher risk devices including lower class devices with serious disease claims. Level 2 audits (Figure 3) verify the application and aspects of the manufacturer's evidence of conformity. Sponsors submit Level 1 documents plus:

- **clinical evidence**
  The manufacturer's Clinical Evaluation Report, Clinical Evaluation Assessment Report produced by overseas regulators, or other clinical evidence or data
- **risk management report**
  Produced by the manufacturer to describe the key risks associated with the medical device and what the manufacturer has done to mitigate these risks.

Additional documents may be requested by exception, based on identified risks and the reason the application was selected for audit. For example:

- technical assessment report - from a comparable overseas regulator
- efficacy and performance data - for devices that disinfect other medical devices
- mechanical safety data - e.g., for patient-matched medical devices
- software design and validation data - e.g., for software as a medical device
- biocompatibility data - e.g., for implantable medical devices with identified risks
- sterility validation data - for sterile devices with identified risks
- viral or prion safety data - for substances of animal origin with identified risks
- medicinal safety or quality data - for devices with a medicinal substance.

The TGA may seek advice about applications from external experts or specialists, such as the Advisory Committee on Medical Devices (ACMD). The ACMD provides independent advice to the TGA on the safety, performance, and manufacturing of medical devices.

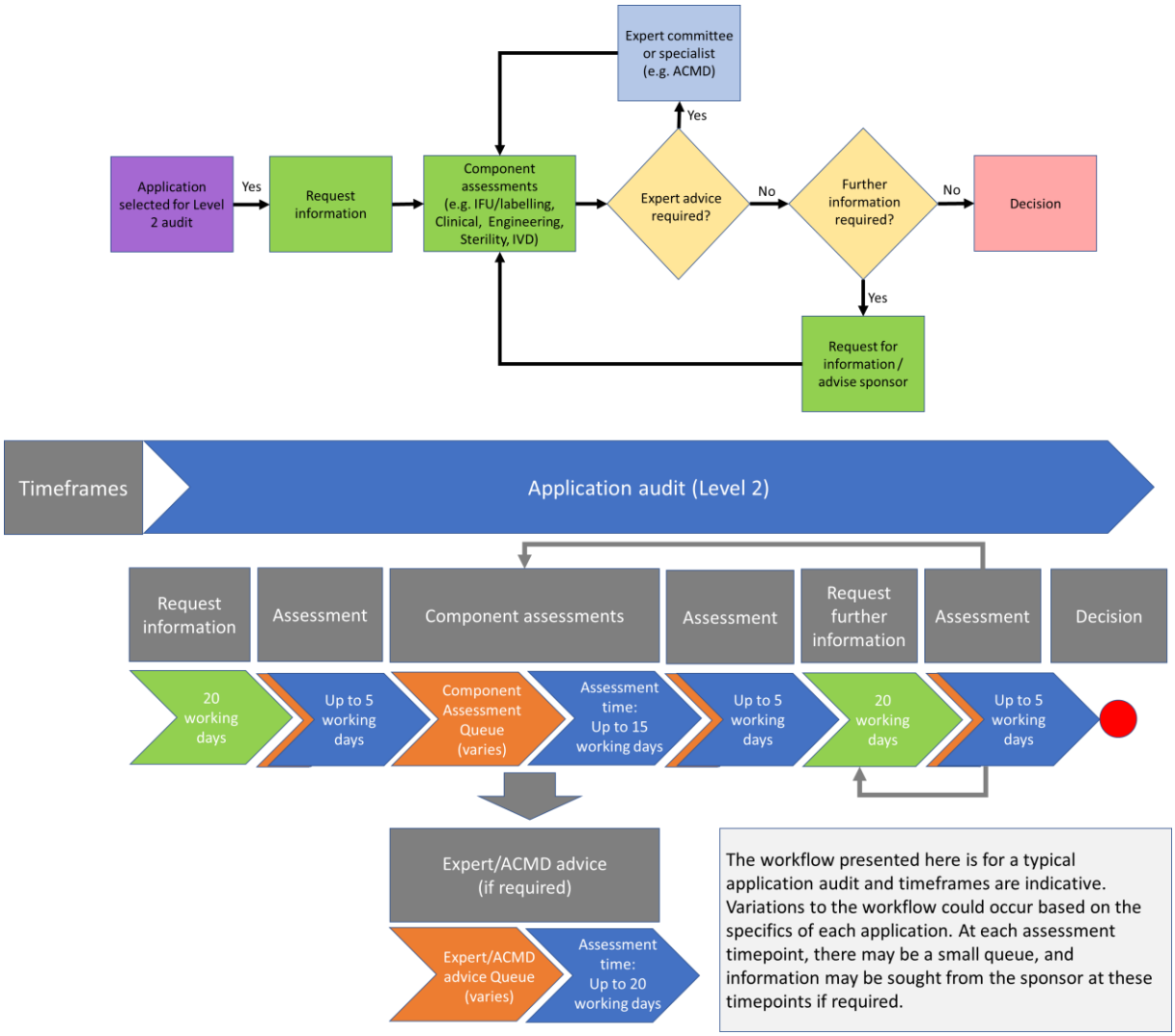


Figure 3: Level 2 application audit workflow

IVD audits

The TGA audits IVD applications with diagnosis claims for a serious disease, where we have concerns about the evidence in the application, or where the test results

have a high public health or personal risk (e.g., self-tests). These are usually for higher risk class devices (e.g., Class 4 IVDs, companion diagnostics). Mandatory IVD application audits are like non-IVD Level 2 audits (Figure 3), and different assessment fees apply for different IVD device classes.

Sponsors are typically required to submit the following for an IVD audit:

- **Clinical evidence**
  Information that supports the clinical utility and the performance of the IVD
- **Performance evaluation reports**
  To demonstrate the clinical and analytical performance of the IVD
- **Risk management report**
  Produced by the manufacturer to describe the key risks associated with the medical device and what the manufacturer has done to mitigate these risks
- **Information to be supplied with the device**.

Additional documents may also be requested, based on the risk:

- design and manufacturing information - appropriate to the IVD device class
- stability studies - to support the stated shelf life
- technical assessment report - from a comparable overseas regulator
- software design and validation data - e.g., for software as a medical device
- post market data.

What we have observed

After the July 2021 Regulation changes, we established interim processes for reviewing EU MDR and IVDR applications. For lower class devices, we treat EU MDR and IVDR applications the same as other applications and select applications for non-mandatory audit based on post market intelligence and information in the application.

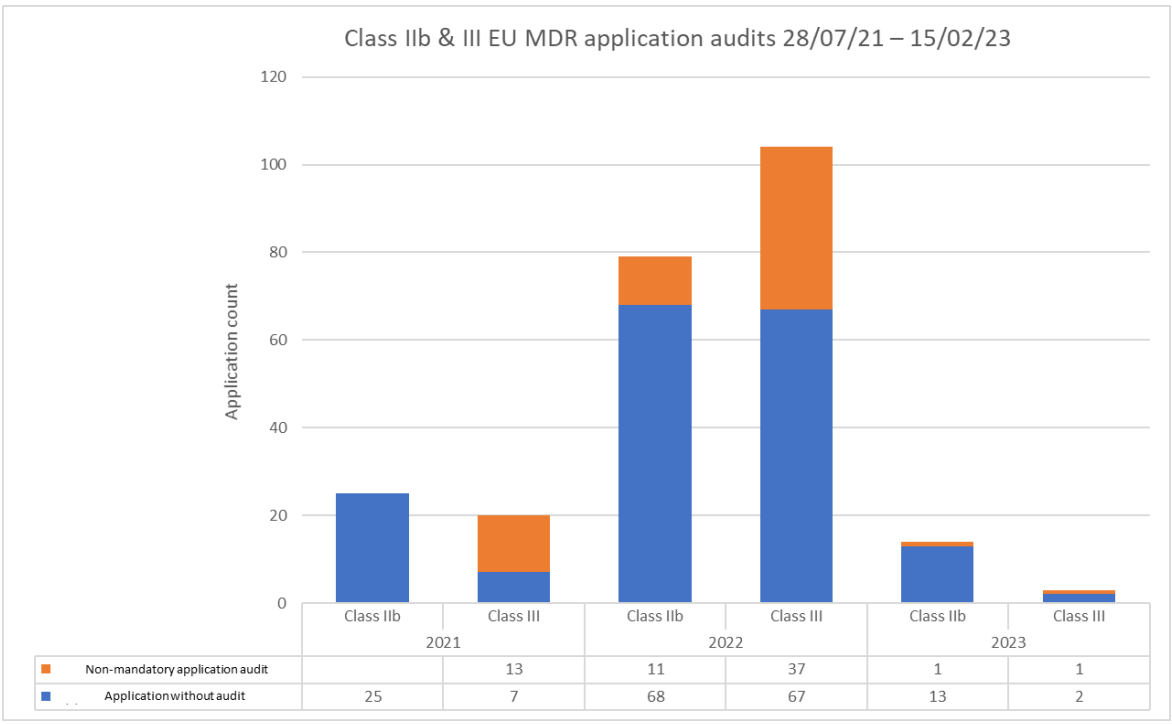
IVD medical devices

To date, the TGA has received a very small number of applications supported by EU IVDR and has not seen any identifiable trends with non-mandatory audits. We have not yet received any Class 4 IVD applications with EU IVDR evidence.

Interim process for non-mandatory audit of EU MDR applications

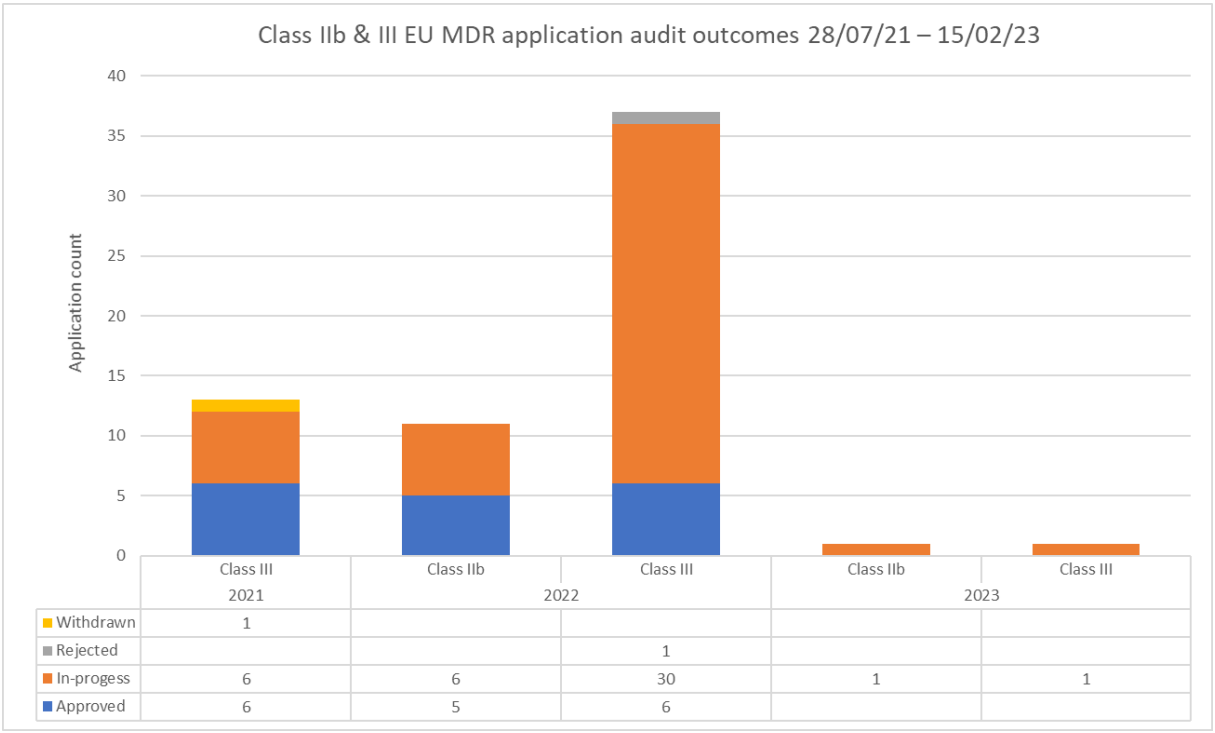
For Class III devices with EU MDR certification, we obtain clinical evidence, Instructions for Use, and the risk management report for the device from the sponsor. We use these documents to triage and select Class III EU MDR applications for non-mandatory audit based on risk.

Since the regulation changes on 28 July 2021, the TGA received 249 Class IIb and Class III EU MDR applications (as of 15 February 2023). The proportion of Class III EU MDR applications selected for non-mandatory audit has steadily declined over time (see Figure 4), with a non-mandatory audit rate of 65% in 2021, down to 36% in 2022. Of the 19 applications completed, 17 were approved, and there were 44 applications still under review (see Figure 5).



	Class IIb 2021	Class III 2021	Class IIb 2022	Class III 2022	Class IIb 2023	Class III 2023
Non-mandatory application audit		13	11	37	1	1
Application without audit	25	7	68	67	13	2
% Selected for audit	0%	65%	14%	36%	7%	33%

Figure 4: Class IIb & III EU MDR application audits 28/07/21 – 15/02/23.



	Class III 2021	Class IIb 2022	Class III 2022	Class IIb 2023	Class III 2023
Withdrawn	1				
Rejected			1		
In-progess	6	6	30	1	1
Approved	6	5	6		

Figure 5: Class IIb & III EU MDR application audit outcomes 28/07/21 – 15/02/23.

Proposed new application audit framework

The proposed new application audit framework will:

- enable a more responsive, risk-based approach to selecting applications for audit, based on post-market signals, regulatory reforms, and regulatory intelligence
- provide more predictability and transparency regarding types of applications likely to be selected for audit, their focus and expected timeframes
- appropriately target regulatory effort
- analyse trends and enable findings to inform advice to industry about the quality of applications and continuous improvement of the audit framework.

Key elements of the proposed new application audit framework are informed by historical and recent trends observed through interim work processes and include:

1. transparency on factors influencing audit selection
2. limiting mandatory audits to highest-risk devices
3. removing mandatory audit requirements for high-risk devices supported by certain comparable overseas regulator approvals
4. requiring documentation at time of submission to inform audit selection
5. exploring pathways for Class III devices supported by MDSAP and US FDA 510(k)
6. limiting the number of substantial assessment rounds
7. improving visibility of application audit timeframes
8. cost recovery mechanisms for non-mandatory audits

Key elements of the proposed application audit framework

1. Transparency on factors influencing audit selection

To provide transparency and certainty for sponsors, the TGA will publish a set of risk factors that influence the likelihood that a medical device will be selected for non-mandatory audit.

The risk factors are dynamic and will be informed and reviewed through periodic environmental scanning of:

- regulatory intelligence and post-market information, such as compliance and enforcement history, results of post-market reviews, and intelligence from other regulators or agencies
- regulatory reforms, such as reclassification of devices, etc.
- situational or environmental risks (such as COVID-19)
- stakeholder concerns about emerging risks
- outcomes of applications and the reasons why applications are withdrawn or rejected.

We propose to review, update, and publish the risk factors on the TGA website every two years, with additional ad hoc updates as required (e.g., due to critical safety signals). The TGA will also report on trends and the types of devices selected for non-mandatory audit and the outcomes of those audits.

The proposed risk factors apply to all medical device applications for inclusion in the ARTG, including all classes of device and IVD medical devices.

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.

Risks relevant to the regulation and approval of the device

The TGA proposes:

- if **a detailed assessment is required to resolve concerns** about the information in the application or supporting documents, or whether the product is a medical device, IVD medical device or is correctly classified, and this cannot be resolved during the preliminary assessment stage, the application may be selected for a non-mandatory audit.
- if there is a deficiency or compliance issue in the application or supporting documentation (e.g., inconsistent or incorrect information, or non-compliance with essential principles), the application may be selected for a non-mandatory audit
- a device approved by **multiple** comparable overseas regulators with the **same intended purpose** is less likely to be selected for non-mandatory audit.

  We propose that sponsors could inform the TGA about additional approvals by attaching evidence with their application for inclusion. Unfortunately, sponsors cannot associate additional comparable overseas regulator approvals with their manufacturer evidence that supports their application.
- if the device is **classified differently in Australia than other countries**, or to support compliance with **recent regulatory reforms**, the application may be selected for non-mandatory audit, if this cannot be resolved during the preliminary assessment stage. For example:
    - software classification differences between Australia and the EU mean some devices classified as Class I in the EU may be a higher class in Australia
    - devices with antibacterial coatings that contain silver, iodine, etc. are Class III in Australia but may be a lower class in the EU
    - the TGA needs to record and assess **details about medicinal substances** in devices
    - patient-matched medical devices require ARTG inclusion in Australia but may be exempt from registration in the EU
    - recent IVD Companion Diagnostics reforms need ongoing support to ensure compliance.

Risks apparent from the quality of the clinical evidence

The TGA proposes the following (for Class III and Class 4 IVD medical devices only):

- **sufficiency of the clinical evidence**
    - regulatory frameworks prescribe when a clinical trial is required, but not what the study should involve or what end points need to be proven.

Where the TGA has concerns about the clinical evidence, the application will be selected for audit.
    - clinical evidence is likely to be considered inadequate when:
        - there is no evidence that any form of systematic, prospective data collection has been undertaken
        - the clinical study's sample size is too small (noting the expected sample size depends on the device type and its intended use)
        - the clinical evidence does not directly relate to the application (i.e., it may apply to a broader range of devices)
        - the evidence is limited to post market vigilance data.
    - applications supported by **lower quality** clinical evidence are **more likely** to be selected for non-mandatory audit. e.g., clinical studies that are not adequately powered, lacking a control arm or where it is not clear that the clinical evaluation relates directly to the device.
    - applications supported by **high quality** direct clinical evidence are **less likely** to be selected for non-mandatory audit. e.g., powered randomised control trial against an appropriate control; or demonstration of widely accepted objective performance criteria fully assessed over an adequate study duration.

- **currency of the clinical evidence**:
    - while the TGA will not undertake a full review of the clinical evidence, we will look at its currency. Where **clinical evidence is not current**, or where there are conditions on overseas approvals requiring the manufacturer to report the outcomes of ongoing clinical studies, the application is **more likely** to be selected for non-mandatory audit.
    - where the certification was recent and the **clinical evidence is current**, an application is **less likely** to be selected for audit. For example, an application with a clinical evaluation report that is dated within 2 years of the application would be less likely to be selected for audit.

- Where a manufacturer claims the device meets the essential principles based on **equivalence** to an existing device in the ARTG, or the application is for a device that has only minor changes from a predicate device that is included in the ARTG:
    - if the TGA can **quickly verify equivalence**, and there are no post-market issues with the approved equivalent devices, we are **less likely** to select the application for audit.
    - If the device has **significant differences compared to its predicate**, which require a detailed understanding to determine the effect on clinical outcomes, the TGA is **more likely** to select the application for audit.

For IVD medical devices:

- the manufacturer must hold clinical evidence that:
    - establishes the current standard of care relevant to the intended purpose and indications for use of the device through review of information related to both **scientific validity** and **clinical performance**; and
    - demonstrates that the **analytical performance** of the device is comparable to the established standard of performance.
- If an IVD test kit claims to be used both in symptomatic and asymptomatic individuals and the performance data to demonstrate clinical sensitivity and

specificity studies in asymptomatic individuals has not been provided, it is **more likely to be selected for audit**.
- If an IVD is for use by patients in self-testing or at point-of-care, and the clinical evidence includes usability and human factors testing data in the applicable user groups, it is **less likely to be selected for audit**.

Risks relating to the sponsor, manufacturer, or type of device

The TGA will consider, for all classes of medical devices and IVD medical devices:

- whether post-market intelligence indicates any concerns about the device type, sponsor, or manufacturer. For example, where:
    - the TGA has cancelled this device from the ARTG before
    - the TGA is aware that this device has been cancelled or refused approval by other regulators
    - the TGA previously rejected an application for this device
    - the sponsor previously withdrew an application for this device and there were unresolved safety, performance, or compliance concerns
    - the manufacturer has other devices in the ARTG that have had post-market issues that are relevant to this specific device
    - the TGA has information about recent quality management system audits of the manufacturer, conducted by a comparable overseas regulator or by the TGA, that found significant non-compliance that may impact the safety or performance of this device
    - the TGA has taken recent compliance action against this sponsor or manufacturer that is relevant to this application.

- risks relevant to the device type and its intended purpose:
    - the same type of device has been associated with well documented serious premarket or post market safety or performance concerns (e.g. implantable contraceptive devices, complex genomic tests)
    - devices to diagnose, prevent or treat emergency diseases (personal protective equipment and COVID-19 tests are recent examples) or diseases with a different impact in Australia than in other countries.

Consultation proposal 1

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.

Consultation 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?

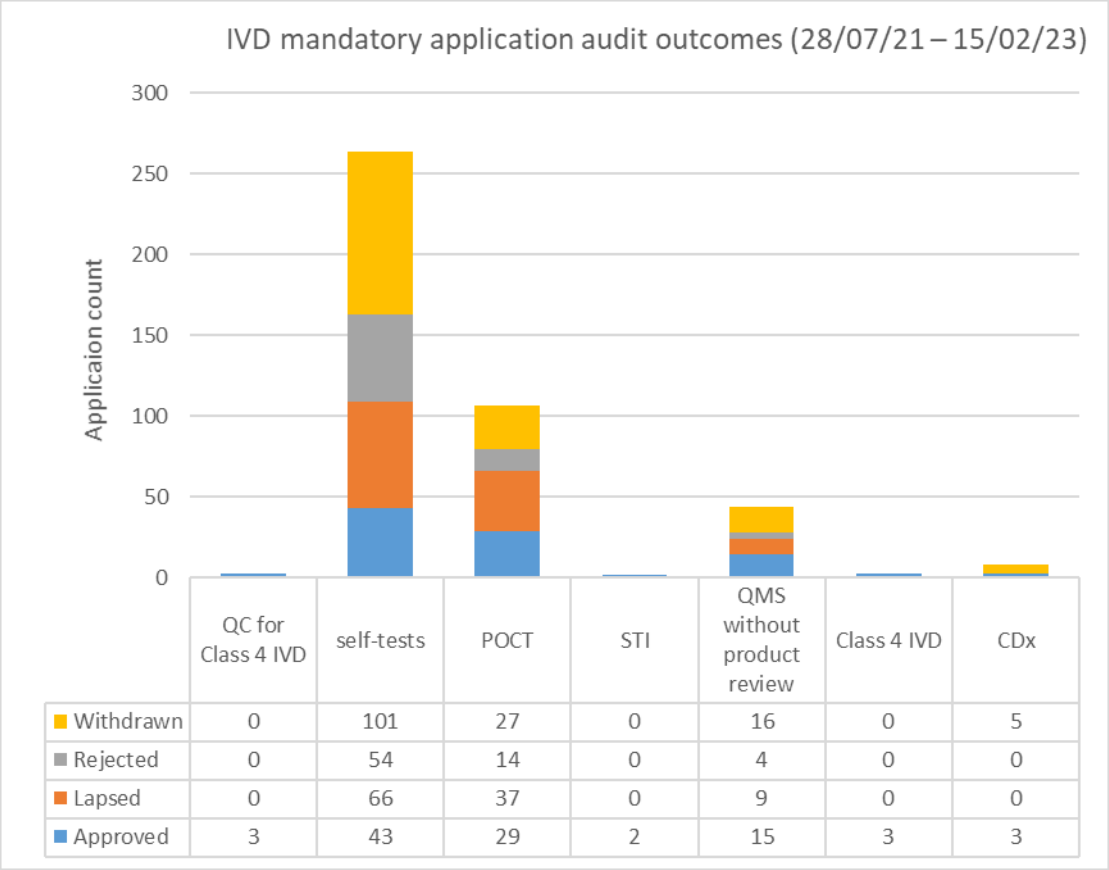
2. Limiting mandatory audits to highest-risk devices

Regulation 5.3 specifies that some types of medical devices must be selected for mandatory audit, unless supported by a TGA conformity assessment certificate, EU MDR or EU IVDR certification. The types of medical devices, including IVD medical devices, that must be selected for audit include:

- a medical device that is:
    - a barrier indicated for contraception or prevention of the transmission of disease in the course of penile penetration during sexual intercourse (other than a condom)
    - an implantable contraceptive device
    - a spinal fusion implantable device (including screws, cages, plates, hooks, or rods used in spinal fusion procedures)
    - specifically intended by the manufacturer to be used for disinfecting another medical device
    - an implantable intra-ocular lens
    - an intra-ocular visco-elastic fluid
    - a Class III medical device.
- an IVD medical device that is:
    - a non assay specific quality control material for monitoring a Class 4 IVD
    - for self-testing
    - for point of care testing
    - to be supplied for use under the pharmaceutical benefits scheme
    - to be supplied for use in a national screening program
    - for managing or monitoring treatment of infections diagnosed with a Class 4 IVD (e.g., quantitative nucleic acid tests and genotyping assays for HIV & HCV)
    - a Class 3 IVD medical device intended for detecting the presence of, or exposure to, a sexually transmitted agent
    - a Class 4 IVD medical device
    - a Class 4 in-house IVD medical device
    - an IVD companion diagnostic.
- an IVD medical device for which:
    - the TGA is not satisfied that appropriate conformity assessment evidence is held to demonstrate that product assessment has taken place. For information on appropriate conformity assessment evidence, see: Use of market authorisation evidence from comparable overseas regulators / assessment bodies for medical devices (including IVDs).

For IVD medical devices, since the July 2021 regulation changes, the TGA has selected 431 IVD applications for mandatory audit (as of 15 February 2023). 61%

were for self-tests, 35% were for point-of-care tests and around 10% were for applications supported by an ISO 13485 or quality management system certificate with no evidence of product review, such as a Canadian Medical Device License. Figure 6 indicates the mandatory audits, the relevant rejection and approval rate.



	QC for Class 4 IVD	self-tests	POCT	STI	QMS without product review	Class 4 IVD	CDx
Withdrawn	0	101	27	0	16	0	5
Rejected	0	54	14	0	4	0	0
Lapsed	0	66	37	0	9	0	0
Approved	3	43	29	2	15	3	3

Figure 6: IVD mandatory application audit outcomes (28/07/21 – 15/02/23)

The TGA is considering developing a proposal to Government to limit the number and types of devices required to undergo mandatory audit. This would move to a more flexible, responsive, and risk-based approach to selecting applications for non-mandatory audit, based on post-market signals, regulatory reforms, and regulatory intelligence. A more flexible framework will allow the TGA to target regulatory effort where it is most needed.

Any recommendation to Government must be based on strong data, intelligence and understanding of risk.

Consultation proposal 2

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
- 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.

Consultation 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?

3. Other comparable overseas regulator approvals

Regulation 5.3 specifies that applications supported by certain regulatory approvals are not subject to mandatory audit (e.g., conformity assessment certification by the TGA, EU MDR and EU IVDR). We seek views about whether there are other comparable overseas regulators that may provide a similar level of confidence, such as Pre-Market Approvals (PMA) by the US FDA.

The TGA has observed a high level of regulatory compliance from medical devices supported by US FDA PMA, noting we continue to build our experience with IVD medical devices supported by US FDA PMA (see Figure 7).

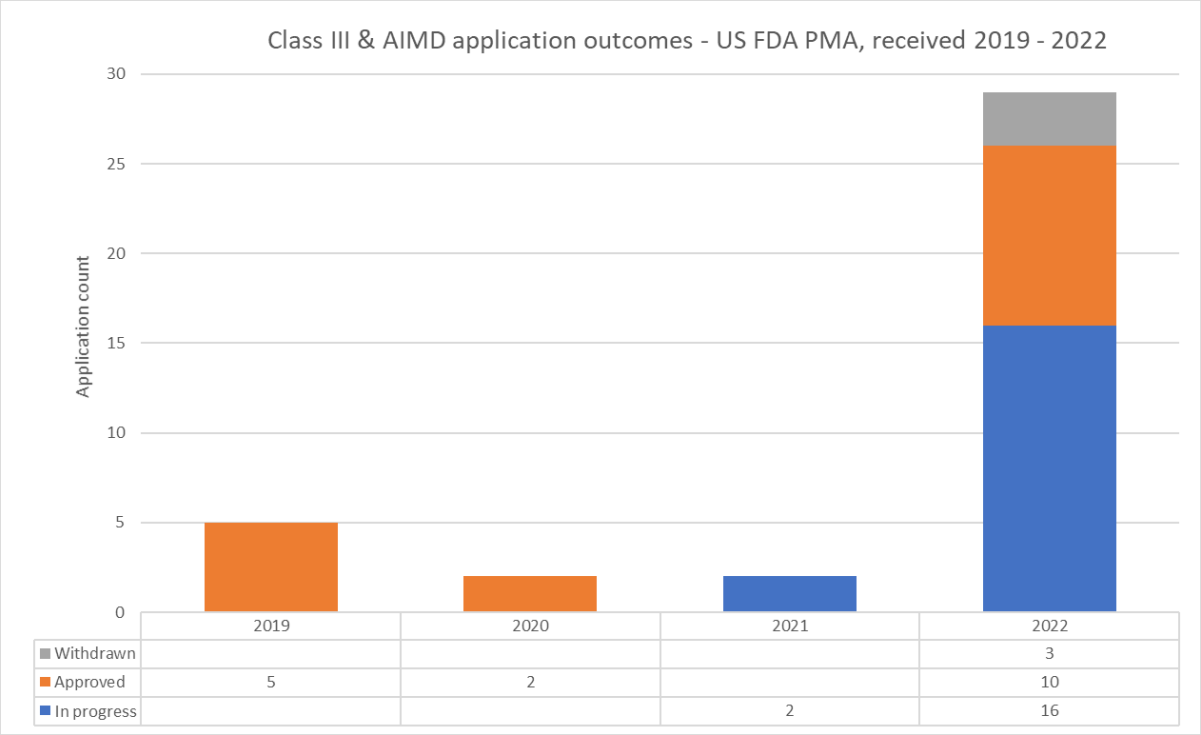


Figure 7: Class III & AIMD application outcomes - US FDA PMA, received 2019-22

If applications supported by US FDA PMA were exempted from mandatory audit, the TGA could still select those applications for non-mandatory audit, in the same way that we can select EU MDR and IVDR applications for non-mandatory audit. Applications supported by US FDA PMA Supplement approval would continue to need to include evidence of the original US FDA PMA. We would also expect that sponsors would need to include the IFU and clinical evidence for the device with any Class III and Class 4 IVD medical device application (see Proposal 5), including those supported by US FDA PMA.

The United Kingdom (UK) is not currently recognised under the TGA's comparable overseas regulator arrangements for medical devices. The TGA has ongoing dialog with the UK Medicines and Healthcare products Regulatory Agency (MHRA) about the UK transition to new medical device regulations and about possible future recognition arrangements in both countries.

Consultation proposal 3

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.

Consultation 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?

4. Pathways for Class III devices with US FDA 510(k)

Some Class III devices in Australia are a lower classification in other jurisdictions, which means that sponsors cannot leverage conformity assessment evidence from comparable overseas regulators. For example, a hip joint metal or polymer constrained cemented system is Class II under US FDA regulations but is a Class III device in Australia. The US FDA 510(k) approval cannot be used to support a Class III application for inclusion in Australia due to the difference in classification. Sponsors therefore need alternative evidence such as EU MDR or TGA conformity assessment certification to support a Class III application in Australia.

The existing pathway for approval in Australia for Class III devices with US FDA 510(k) is TGA conformity assessment certification. We can abridge the assessment in these cases, particularly if the manufacturer also has MDSAP certification to address quality management system requirements. The TGA then needs to assess the safety and performance of the product, including the clinical evidence, via design examination. This pathway also requires two applications to the TGA: first for conformity assessment and then for inclusion in the ARTG. This adds administrative burden and delay.

Any new pathway that required only a single application to the TGA would need to address both the quality management system and product assessment requirements for a Class III medical device, and the costs of that assessment would need to be recovered via an appropriate fee.

Any new pathway needs to be weighed against the existing pathway of an abridged TGA conformity assessment application.

Consultation proposal 4

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.

Consultation 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?

5. Providing evidence to inform audit selection

Since the changes to Regulation 5.3, the TGA began asking for the following additional information for all Class III medical device and Class 4 IVD applications supported by EU MDR or IVDR certification:

- the Instructions For Use (IFU) – i.e. the information provided by the manufacturer to inform the user of the intended purpose of a medical device, about its correct use and any precautions to be taken
- the Clinical Evaluation Report (the CER) – i.e., the manufacturer's summary of clinical evidence for medical devices. For IVDs, clinical and analytical performance reports.

These documents allow the TGA to target devices for non-mandatory audit and reduce the number of devices selected.

The evidence submitted by the sponsor with the application for inclusion informs the scope of a mandatory audit or the selection for non-mandatory audit. This evidence can provide the TGA with important information about the approvals that have already been granted for the device, the characterisation of the device, the intended use of the device and the clinical and other risks that have been identified in connection with the device.

When requesting evidence to be provided in support of an application, the TGA needs to consider the value of this information against the burden that it imposes on the sponsor to submit the information. Requesting more evidence can increase the TGA's confidence in its preliminary risk assessment of the device during the initial

application triage phase. This will reduce the likelihood of a device being selected for non-mandatory audit where this might otherwise be necessary because of inadequate information to inform a risk assessment. However, where more evidence is provided or requested, this increases application compliance costs for all parties.

The *Therapeutic Goods (Medical Devices—Information that Must Accompany Application for Inclusion) Determination 2018* details the conformity assessment documentation that must accompany an application for inclusion, based on device classification.

Depending on risk factors, further information may be requested from sponsors to inform assessment and audit selection.

Between 28 July 2021 and 15 February 2023, the TGA received 131 Class III medical devices supported by EU MDR certification. The TGA selected 51 applications (39%) for non-mandatory audit. Of the remaining 80, 4 applications were yet to be reviewed and the remaining 76 applications (58%) were approved without audit within the 20-day statutory timeframe.

Further analysis indicated a downward trend in the non-mandatory audits of EU MDR supported applications (see Figure 4). The TGA estimates that in the longer term, the non-mandatory audit rate may trend towards 15% for Class III applications supported by EU MDR certification, following a triage of the application, IFU and CER.

To date, we have received a very small number of applications supported by IVDR certification, so we do not have sufficient experience to inform any identifiable trends. The proposal for IVDR supported applications is based on the experience with the MDR supported applications.

While the requirement to submit the IFU and CER imposes an impost on the sponsor, the experience so far suggests that sponsors have ready access to these documents for Class III devices, noting that sponsors are legally required to have access to these documents. IVD clinical and analytical performance evaluation reports should similarly be readily accessible for Class 4 IVDs.

Given the importance of the IFU and the CER in informing the TGA's risk assessment, the TGA also considered whether such documents should be routinely required as part of applications for lower class devices and sought the advice of the TGA's Regulatory and Technical Consultative Forum for Medical Devices (RegTech). Informed by that advice, the TGA considers that the lower risk and high volume of devices in these other classes does not warrant the regulatory burden associated with routinely requiring these documents. Similarly, we are not proposing that sponsors provide the EU Notified Body Clinical Evaluation Assessment Report for Class III medical device applications.

Recognising that some CERs are significant in size, the TGA will explore improvements to the way this information is provided to the TGA (e.g. through the existing GovTeams portal, and through improved submission portals under the TGA digital transformation project). We will also explore ways to ensure the CER includes

a Table of Contents or bookmarks to reduce the time needed for the TGA to quickly triage the document for audit selection.

Consultation proposal 5
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.

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

6. Limiting the number of substantial assessment rounds

To reduce application queues and assessment timeframes, we plan to restrict medical device and IVD application audits, for all classes of device, to two substantial review rounds. If there are multiple component assessments, each substantial review round means one round of assessment of all the relevant components. Additional review rounds would be by exception only, under limited circumstances, such as to provide an opportunity to respond to advice from the Advisory Committee on Medical Devices.

Figures 1 to 3 outline the application review process, which may include multiple clinical and other assessment rounds (e.g., biomaterials, engineering, IVD, etc.). A significant number of applications have insufficient evidence to substantiate compliance, resulting in multiple (3-5) rounds of requests for information and subsequent assessment of that information. This impacts the time to finalise the application and takes TGA resources away from reviewing and processing other applications.

We propose a modified process, detailed in Figure 8. At the end of the first round, we plan to advise the sponsor of the issues identified and give them the opportunity to address the issues. Sponsors may seek to discuss the issues with us via a phone or video call before responding. If the information provided in response is insufficient to demonstrate compliance, we would advise the sponsor that the application may be rejected, and sponsors may then opt to either withdraw or proceed with the application.

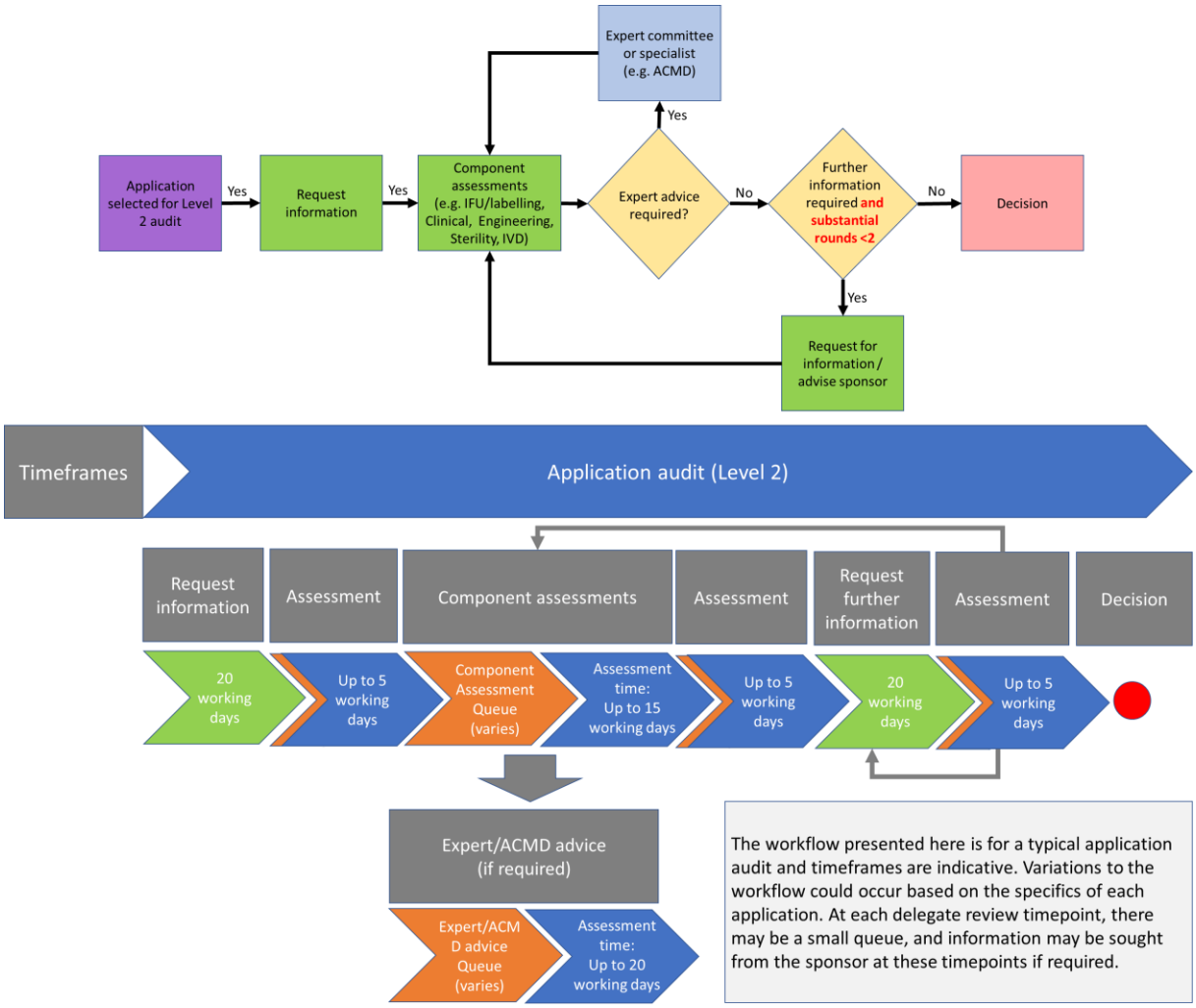


Figure 8: Level 2 application audit workflow, with a limit of 2 substantial review rounds

Consultation proposal 6
We will limit the number of substantial review rounds to two, with any additional (substantial) rounds to be by exception only.

Consultation question 6
Do you have feedback about further measures to improve assessment timeframes?

7. Improving visibility of application audit timeframes

The TGA has received feedback that sponsors want increased visibility of the status and timeframes for all application audits of medical devices, including IVDs.

An example of improved timeframe visibility would be for the TGA to inform applicants of the expected processing time for their application, updated at key milestones in the process. For example, at the time of submission, we could inform the applicant that they can expect an X-day time for completion, based on average performance at that time. We could inform the applicant a revised expected

completion time at subsequent milestones in the process, such as when the application joins the clinical assessment queue.

Any interim system to provide timeframe visibility will need to be weighed against the TGA digital transformation project and what that will deliver. The benefits will need to be balanced against the work effort and cost to produce and maintain the system.

We welcome feedback on the information you would like us to provide applicants.

Consultation proposal 7

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

Consultation question 7

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

8. Recovering the costs of non-mandatory audits

The TGA is not planning to implement fees to undertake non-mandatory application audits.

Provided the numbers of non-mandatory audits do not substantially increase from the existing numbers, there should be no change to future fees and charges. The TGA will monitor the number and depth of non-mandatory audits it undertakes and consult with industry on any future impact to costs.

What we invite you to do

In your submission, we ask you to consider and respond to the questions below, and to provide comments on the issues outlined in this consultation paper.

Consultation questions (consolidated)

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?

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?

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?

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?

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

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

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

How to submit your feedback

Your input and feedback will help inform the development of the proposed new application audit framework for medical devices. In addition to the scope of this consultation, we welcome feedback on our consultation process.

You can review the consultation on our consultation hub and submit your feedback by email response to devicereforms@tga.gov.au

Participation and feedback provided during this consultation is greatly appreciated.

Following internal review of feedback received and approval, the consultation outcomes will be published on the TGA website. This is expected to occur in late 2023.

Please direct any queries via email to devicereforms@tga.gov.au.

This survey closes at 23:59pm on 04/09/2023

Version history

Version	Description of change	Author	Effective date
V1.0	Draft for stakeholder feedback	Medical Devices Authorisation Branch	April 2023
V2.0	Public consultation	Medical Devices Authorisation Branch	July 2023

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Reference/Publication #