Regulatory update from the Medical Devices Surveillance Branch

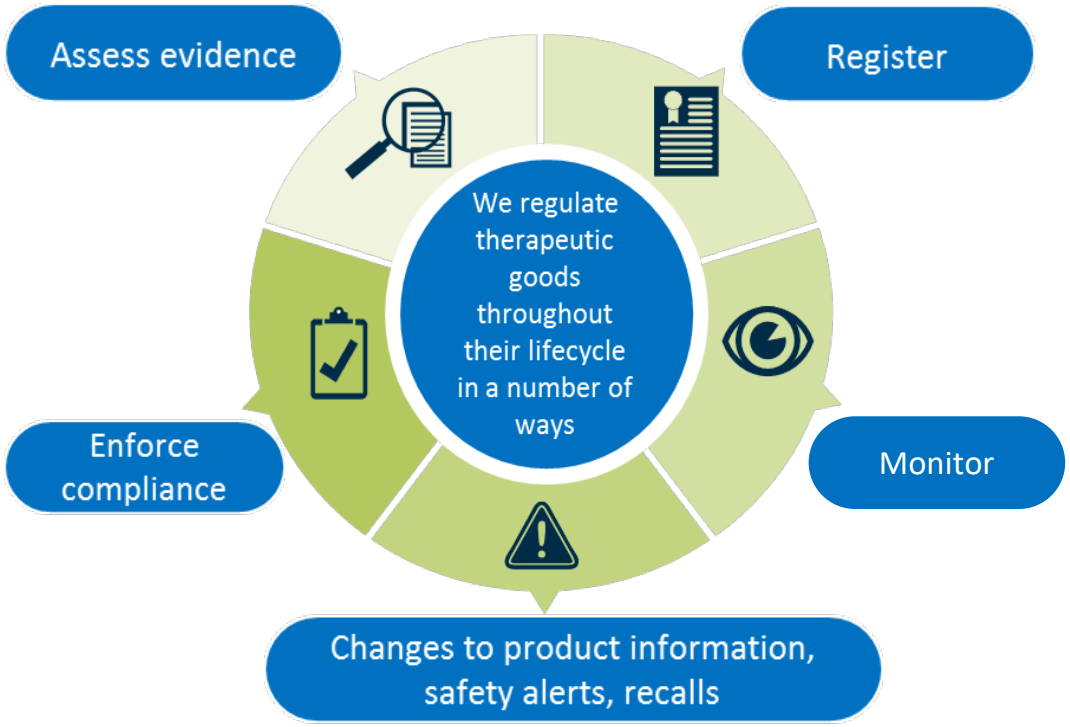
Dr Kelly Tsang
Acting Director, Devices Post-Market Monitoring Section
Medical Device Surveillance Branch
Department of Health and Aged Care, TGA

Part 1

Adverse events and annual reports refresher

- Ongoing obligations for sponsors and manufacturers
- Definitions and requirements for reporting of adverse event
- TGA activities in response to adverse events
- Requirements for annual reporting and additional conditions of inclusion

Regulating throughout the lifecycle



Post-Market Obligations

- Post-market performance is monitored for trends or issues not previously known.
- Medical devices are subject to conditions of inclusion.
- Medical devices can be subjected to post-market review or investigations at any time.
- Summary available on the TGA website

Manufacturer responsibility

Manufacturer - the person who is responsible for the design, production, packaging and labelling of the device before it is supplied under the person's name

- Allow entry and inspections of premises
- Demonstrate compliance with essential principles
- Demonstrate and maintain compliance with conformity assessment procedures (CAP)
- Notify TGA of substantial changes in design, production or changes to CAP
- Maintain records of complaints, adverse event records and post-market action
- Undertake investigations and implement actions based on post-market experience, including recalls

Sponsor responsibility

Sponsor - person who arranges for import, export and supply of therapeutic goods in Australia

- TGA's point of contact for regulation, legal entity for post-market action
- Arrange for import/ export/ supply of goods in Australia
- Have written agreement with manufacturer to obtain information when requested by the TGA
- Deliver samples upon request
- Facilitate Australian recall actions
- Comply with the Therapeutic Goods Advertising Code
- Pay annual charges

Examples of TGA post-market activities

The TGA has a variety of processes for managing ongoing compliance

- Device incident reports
- Product investigations or post-market review
- Desktop and/ or on-site inspections
- Review annual reports (Class IIb implantable, Class III and Class 4 IVD)
- Impose / vary additional conditions of inclusion
- Consent to Supply products that don't meet Essential Principles
- Recall actions
- Ongoing surveillance and exchange of information with other agencies, international regulators / notified bodies.

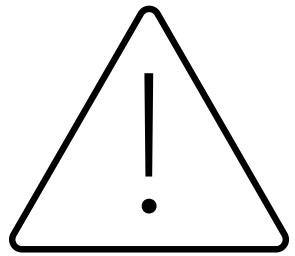
What is an ‘adverse event’?

- An event that resulted in serious injury, illness or death to patient, healthcare worker or other person.
- A medical device adverse event is an event associated (caused or partially attributable) with the use (or misuse) of a medical device.
- Faults that may affect the quality, timeliness and cost-effectiveness such as, problems with getting the device to operate, repeated repairs, device design and difficulty of use.

What is a ‘near adverse event?

- An event that could have resulted in (had effective intervention not taken place) serious injury, illness or death to patient, healthcare worker or other person.

- For an event to be defined as a near adverse event:
  - ✓ An event associated with the device occurred
  - ✓ If the event occurred again, it might lead to death or serious injury



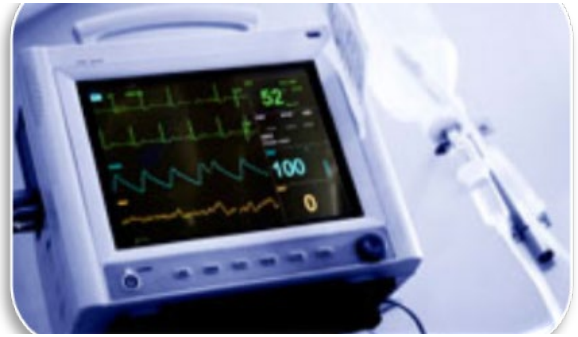
What is a serious injury?

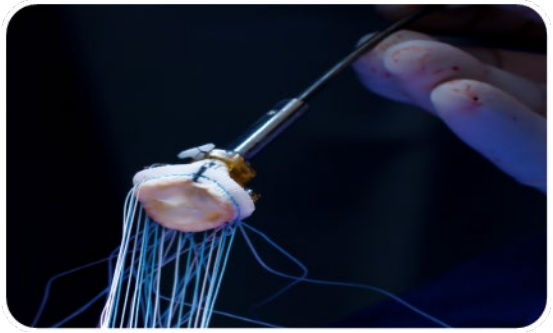
Serious injury (serious deterioration in state of health) is:

- A life threatening illness or injury
- A permanent impairment of a body function (Irreversible impairment or damage to a body structure of function)
- Permanent damage to a body structure
- A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure

Sponsor – mandatory reporting obligations

- Sponsors must report the details of events associated with their medical device(s) that have resulted, or could have resulted, in serious injury or death
- 41MP & 41MPA refers to reporting information related to malfunction or deterioration in characteristics or performance of a device
- Conditions of inclusion
  - *Therapeutic Goods Act 1989* (41FN(3),(d) and 41MP(2) & 41MPA)
  - *Therapeutic Goods (Medical Devices) Regulations 2002* (Reg 5.7)





It is often difficult to determine whether an adverse event was caused by a medical device.

- Causality of the event does not need to be established at the time of reporting
- When in doubt it is better to report than not to report

When to report (Reg 5.7)

- Within **2 days** of becoming aware of an issue of serious public health threat or concern that will require prompt action to reduce the hazard
- Within **10 days** of becoming aware of a death or serious injury
- Within **30 days** of becoming aware of an event that might have led to serious injury or death
- Within **60 days** of becoming aware of the lapsing or revocation of a conformity assessment certificate

When to finalise the report (Reg 5.8A)

- It is now a legislative requirement to provide the final report within 120 days of first reporting to the TGA.
- The report must include
  - ✓ Any updates to the original information since that information was given
  - ✓ Details of actions taken to investigate the event or other occurrence concerned
  - ✓ Details of actions taken to alleviate the impact of the event or other occurrence concerned for patients or users
  - ✓ Details of similar events or occurrences in the last 3 years

What to include in the report?

Sponsors of medical devices must provide:

- Clear details of the adverse event
- ARTG entry number for the device
- Device name
- Findings of the manufacturer’s investigation into the event
- Corrective and preventative actions taken
- Details of similar events for the last 3 years (these may be provided in the form of a rate or as a number of similar incidents (clinical observation) over the last 3 years together with the number of devices supplied in that same period). Separate rates for Australia and worldwide to be provided.

Report to IRIS

Incidents/adverse events associated with

- Medical devices included in the Australian Register of Therapeutic Goods (ARTG)
- Medical devices exempt from inclusion on the ARTG e.g. personalised, custom made
- Other Therapeutic Goods e.g. Tampons, Disinfectants

- Devices supplied as part of a clinical trial*
- Devices supplied under Special Access Scheme**
- Devices supplied under Authorised prescriber scheme**

Note: adverse reactions associated with vaccines, medicines and biologicals should be reported to Medicines –see AEMS guidance for sponsors on the TGA Website

What happens to the report?

- Reports are entered into the IRIS database
- Focus is on urgent reports, unusual problems, potentially serious problems, or problems that have high levels of incidences
- After risk assessment the level of investigation is determined
- The manufacturer has primary responsibility to investigation and take action based on their QMS
- Many reports are not investigated by the TGA, however they are utilised for trending and monitoring purposes
- Most reports are placed onto the Database of Adverse Event Notifications (DAEN)

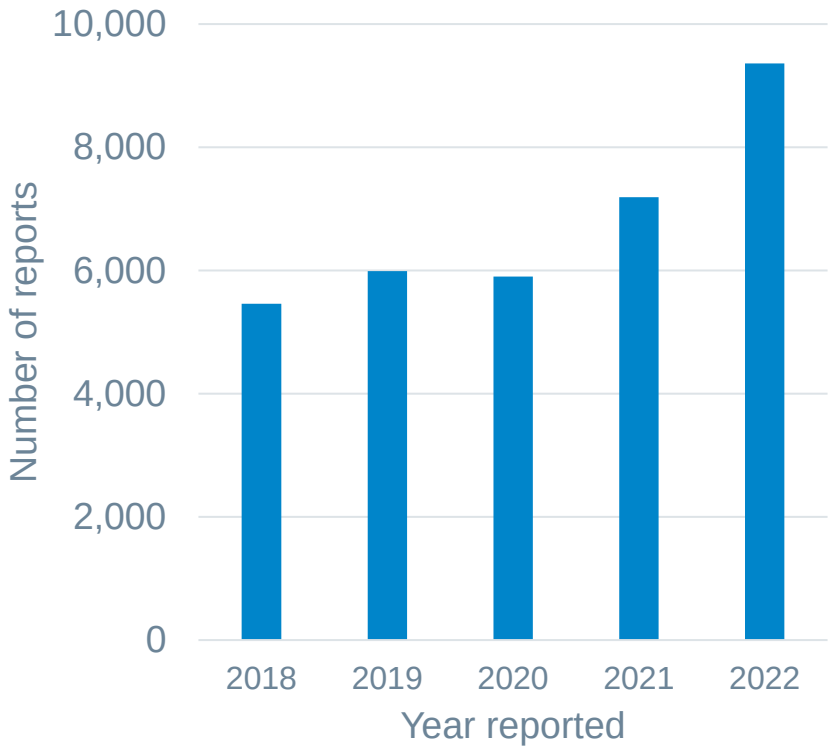
Potential outcomes of investigations

- Safety alert
- Hazard alert
- Recall
- Information on TGA website
- Product and labelling improvements (updating Instructions for Use)
- Increasing post-market surveillance

- Imposing limitations on the medical device's use
- Investigating manufacturing sites
- Suspending or cancelling the product from the ARTG
- Referral to other TGA sections for other regulatory actions

Future of adverse event surveillance

- The TGA received ~300 reports annually when first implemented market surveillance activities, now >9,000 reports per year
- Additional sources from state and territory mandatory reporting
- How do we effectively manage risk to patients and users in the face of increased reporting?
  - data analytics and trending
  - analysis of adverse event outcome experience
  - focused risk assessment on specific report source or risk criteria
  - focus on non-compliance (e.g. lack of reports)
  - decreased manual risk assessment and increased investigation



Annual reports - automatic condition of inclusion

Review of experience gained in post-market

- Annual reports are required to be submitted for the first 3 years of inclusion for Class IIb implantable, Class III devices or Class 4 IVDs.
- Due by 1 October each year
- Non-compliance may lead to cancellation from the ARTG.
- Further information and template available at https://www.tga.gov.au/resources/resource/guidance/annual-reports
- Ongoing work on content and how reports are submitted to reduce the admin burden

Additional conditions of inclusion

Processes to monitor ongoing safety issues

- Additional COIs can be imposed at the time of inclusion, or later
- Allow ongoing monitoring of information and evidence
    - E.g. submit the results of the clinical study and the manufacturer's analysis of the study, as well as any updates to the clinical evaluation report.
- Sponsors should ensure timely receipt of information from manufacturers Ensure there are channels to receive information from manufacturer, and to generate relevant records to demonstrate compliance
- Non-compliance may lead to further regulatory action.

Summary

- Establish communication channels with manufacturer for:
  - Passing on complaints and annual reports
  - Requesting further information- TGA requests, investigations, evidence of compliance
  - Ensuring regulatory timeframes and obligations are met
- Manufacturers have primary responsibility for investigating complaints and AEs
  - TGA may ask sponsor further questions based on risks and trends
  - Sponsors to provide initial and final reports of incidents to the TGA within timeframes
  - If in doubt- contact us or submit a report anyway

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Questions?

www.tga.gov.au

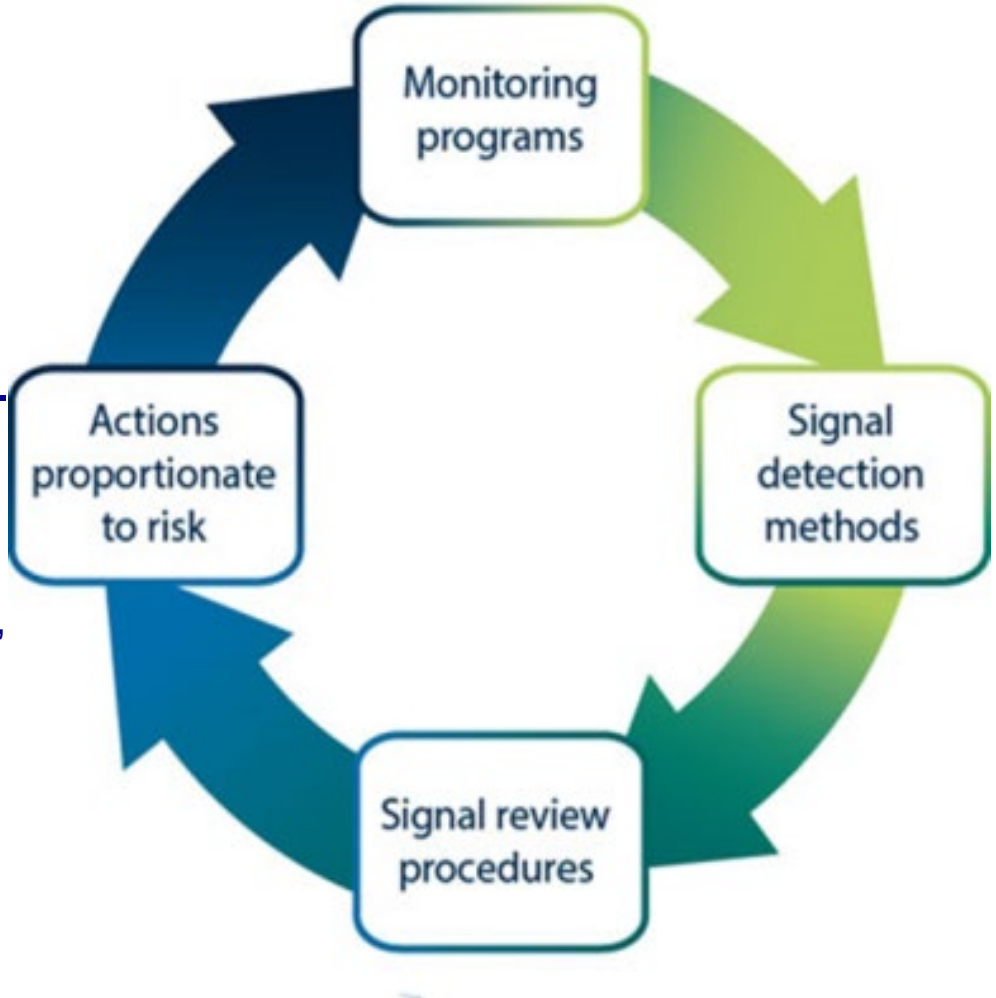
Post Market Reviews Considerations for medical device sponsors

Dr Amanda Craig
Director
Devices Post Market Reforms and Reviews Section
Medical Devices Surveillance Branch
Department of Health and Aged Care, TGA

Post-market reviews are conducted by the TGA to ensure a medical device continues to meet legislated requirements

Post-market obligations

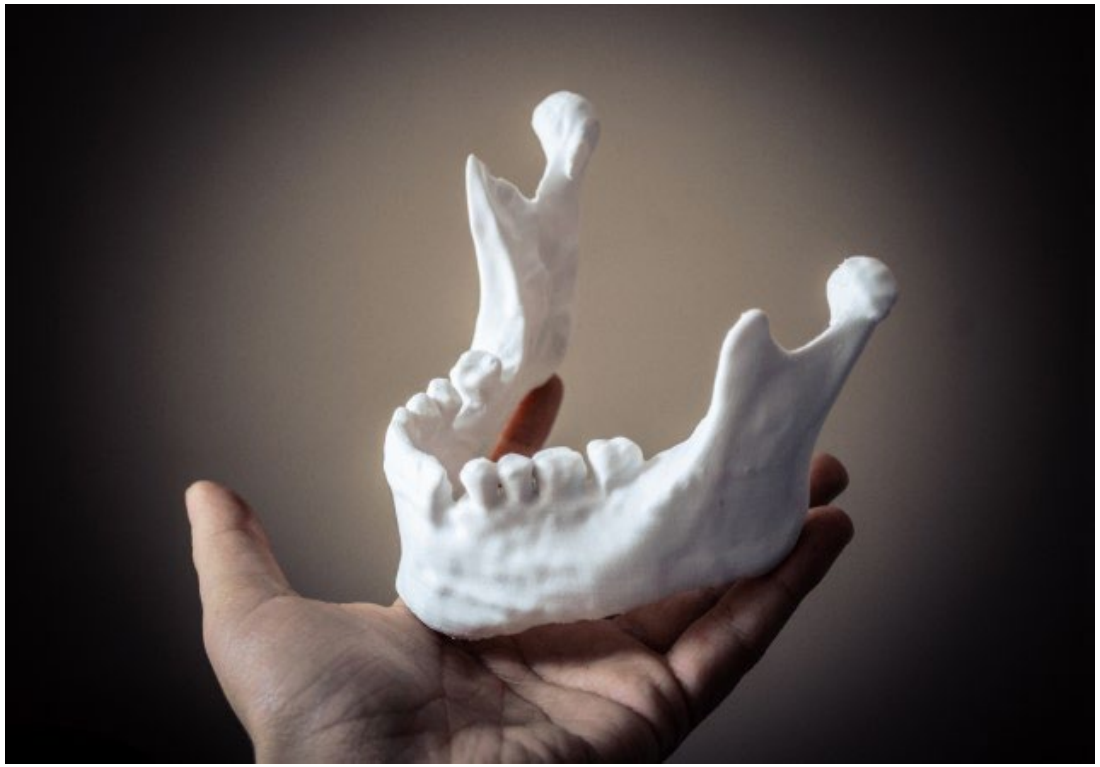
- ARTG inclusion is just the beginning
- Devices can be subjected to post-market review or investigations at any time.
- Post-market performance is monitored for trends or issues not previously known to manufacturers.
- Devices are subject to conditions of inclusion such as:
  - Ensuring continued compliance with the EPs and CAPs,
  - reporting adverse events,
  - providing information and samples,
  - reporting annually for higher classes of device.



Selection for Post-Market Review

There are numerous reasons a product may be selected for post-market review including, but not limited to, the following:

- Detection of a trend or signal amongst post-market data. This data can include, but is not limited to, adverse event reports, annual reporting, clinical publications.
- Information received from, or action taken by, other medical device regulators.
- Identification of a safety or performance issue for a similar device currently included in the ARTG.
- Unresolved or repeated recalls.
- Literature review of available clinical evidence.



SPEAR process

Signal	• Regulators • Adverse events
Planning	• What information do I need? • Time frames?
Evidence	• s41JA and samples • ACMD
Action	• Feedback • Enforcement/Regulatory Action
Report	• Sponsor report • Recommendations to committees or standards

Post-market review: Types of evidence reviewed

AUSTRALIA

Therapeutic Goods (Medical Devices) Regulations 2002

Statutory Rules No. 236, 2002

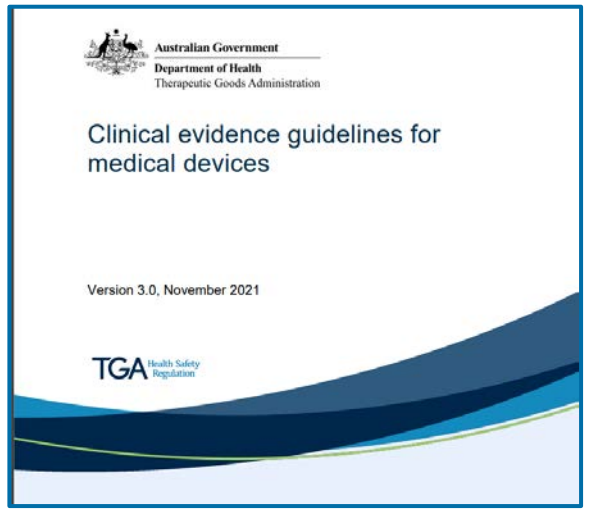
made under the

Therapeutic Goods Act 1989

INTERNATIONAL STANDARD **ISO 13485**

Third edition
2016-03-01

Medical devices — Quality management systems — Requirements for regulatory purposes



INTERNATIONAL STANDARD **ISO 14971**

Second edition
2007-03-01

Medical devices — Application of risk management to medical devices

Specific kinds of data we may request

- Risk analysis
- Risk management
- Root Cause and Corrective and Preventative Actions
- Clinical evidence
- Test evidence
- Advertisements and labelling
- Adverse event reports
- Supply information
- And more….

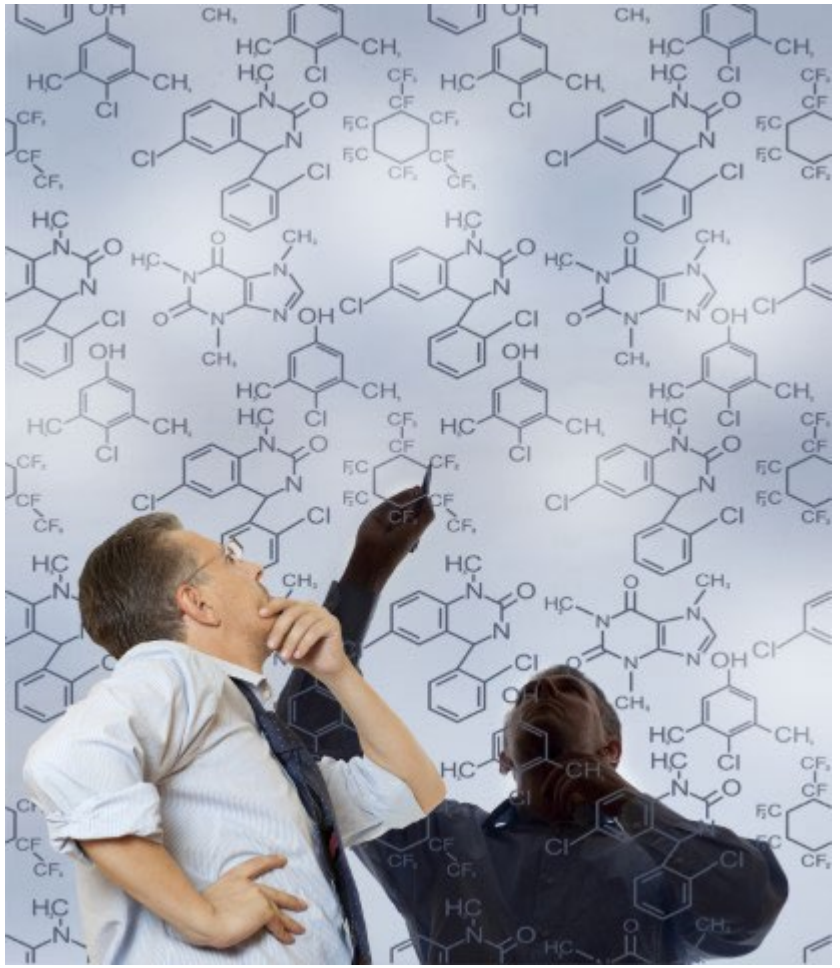
Case Study Example (not an actual case)

- The TGA are reviewing the long-term safety of a Device known as ‘Stimulators r us’.
- A total of 400 devices have been implanted in the past 2 years.
- The TGA received 232 adverse event reports of the device providing insufficient stimulation resulting in surgical revision.

What kinds of post-market evidence would you expect the TGA to require?

Types of information we expect

- Evidence that supports the **entire lifespan** of the device with regard to:
  - Adverse event/complaint/CAPA
  - Risk analysis/FMEA
  - Safety (clinical trials, test evidence)
  - Biocompatibility (where possible)
  - Functional outcomes – Intended purpose
  - Population reflects the claims on the IFU
  - Post-market studies post implantation (quality of life)



Thought process in Post-Market

- Based on the reports, the revision rate of these implants is 58%
- The total adverse events (surgical revisions) (232) is unacceptably high compared to the total amount of implants (400)

<u>Questions we may have</u>

- What procedures does the manufacturer have in place to minimise this risk?
- What is the root cause of the issue?
- How long has this occurred for?
- Are there unaccounted cases?
- What immediate action can we take to minimise this harm?

Risk Management – What does it look like?

Identify
- Risks to management operations

Assess
- Analyse major risks to determine course of actions

Treat
- Breaks down methods to mitigate and reduce risks

Monitor
- Monitor and report on findings

Scale	Likelihood/occurrence	Harm/Severity
1	>1 in 1,000,000 events per year	No injury or damage
2	>1 in 100,000 events per year	Some first aid required
3	>1 in 10,000 events per year	External non-life threatening injuries
4	>1 in 1,000 events per year	Extensive life-threatening injuries
5	>1 in 10 events per year	Death or Major injury resulting in intubation

Case Study Example – Emerging Risks

- SARS-CoV-2 emerged late 2019 with the wildtype (Wuhan strain)
- Kits are designed against SARS/SARS-CoV-2 wildtype strain
- New variants emerge over time (Omicron, Delta)

Important – risk may change throughout lifecycle!

What do we expect?

Proactive monitoring! COVID-19 test kit specific example

- Identify the risk – Mutations present in emerging variants may impact sensitivity of test kit

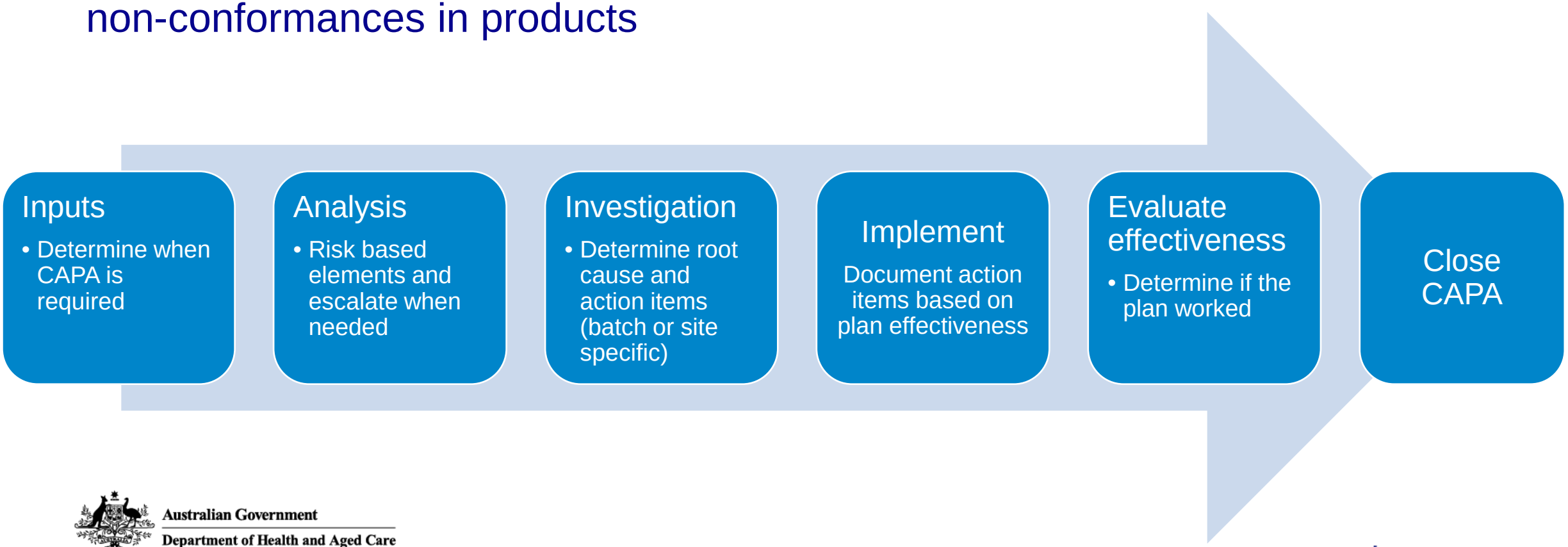
- Identify the potential harm – false negative results, delayed detection

What do we expect – Cont.

- Identify the outcome – Delayed detection or false negatives may lead to patient infection and spread in the community
- Mitigate the risk - Put processes in place to address and mitigate the risk as far as possible. This may include undertaking in-silico analysis, wet-lab testing, clinical testing.
- Continue to monitor the risk – Continue to monitor adverse events, literature evidence, media, genomic surveillance databases to remain abreast of any new variants.

Root Cause Analysis and CAPA

Identification and elimination or reduction of existing or potential non-conformances in products



Post-market review outcomes

- Closure of review
  - Not in scope
  - Sufficient and satisfactory evidence provided
- Amendment to Instructions for Use
- Recall of devices or safety notice
- Additional conditions of inclusion (s41 FP)

- Suspension (s41 GA & GF)
- Cancellation (s41 GK, GL, GM, & GN)
- Infringement notices
- Referral to:
  - Advertising Compliance (s42 DL) or
  - Regulatory Compliance

Uniform Recall Procedure for Therapeutic Goods (https://www.tga.gov.au/sites/default/files/uniform-recall-procedure-therapeutic-goods-urptg.pdf)

If in doubt – contact us

Devices contact team
devices@health.gov.au
1800 141 144

Reforms
devicereforms@health.gov.au

Incident reporting
IRIS@health.gov.au
1800 809 361

Post-market reviews
postmarketdevices@health.gov.au

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Department of Health and Aged Care

Therapeutic Goods Administration

Regulatory Update from the Medical Devices Surveillance Branch

Maria Ong
Director, Devices Vigilance and Policy Section
Medical Devices Surveillance Branch
Department of Health and Aged Care, TGA

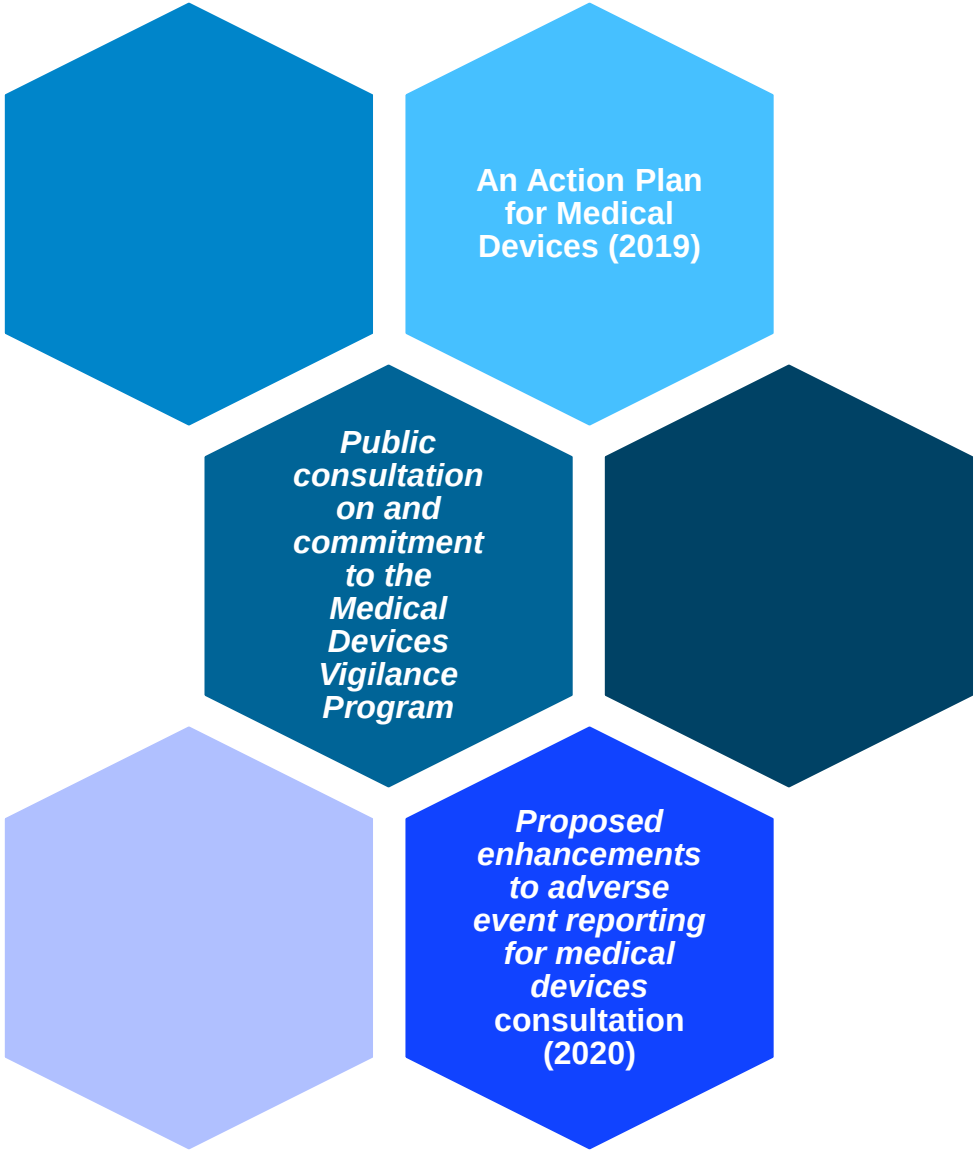
Medical Devices Vigilance Program

Background

Action Plan for Medical Devices

TGA 2020 consultation paper – industry and consumer feedback supported implementing such a program to:

- **educate and promote** better regulatory compliance among sponsors
- **reinforce** the requirement to hold timely and accurate information, and
- **ensure compliance** to requirements, whilst identifying areas for improvement.

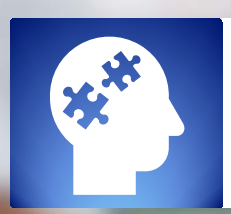


MDVP Objectives

Improve understanding of regulatory obligations

Reinforce medical device sponsors' regulatory obligations and requirements

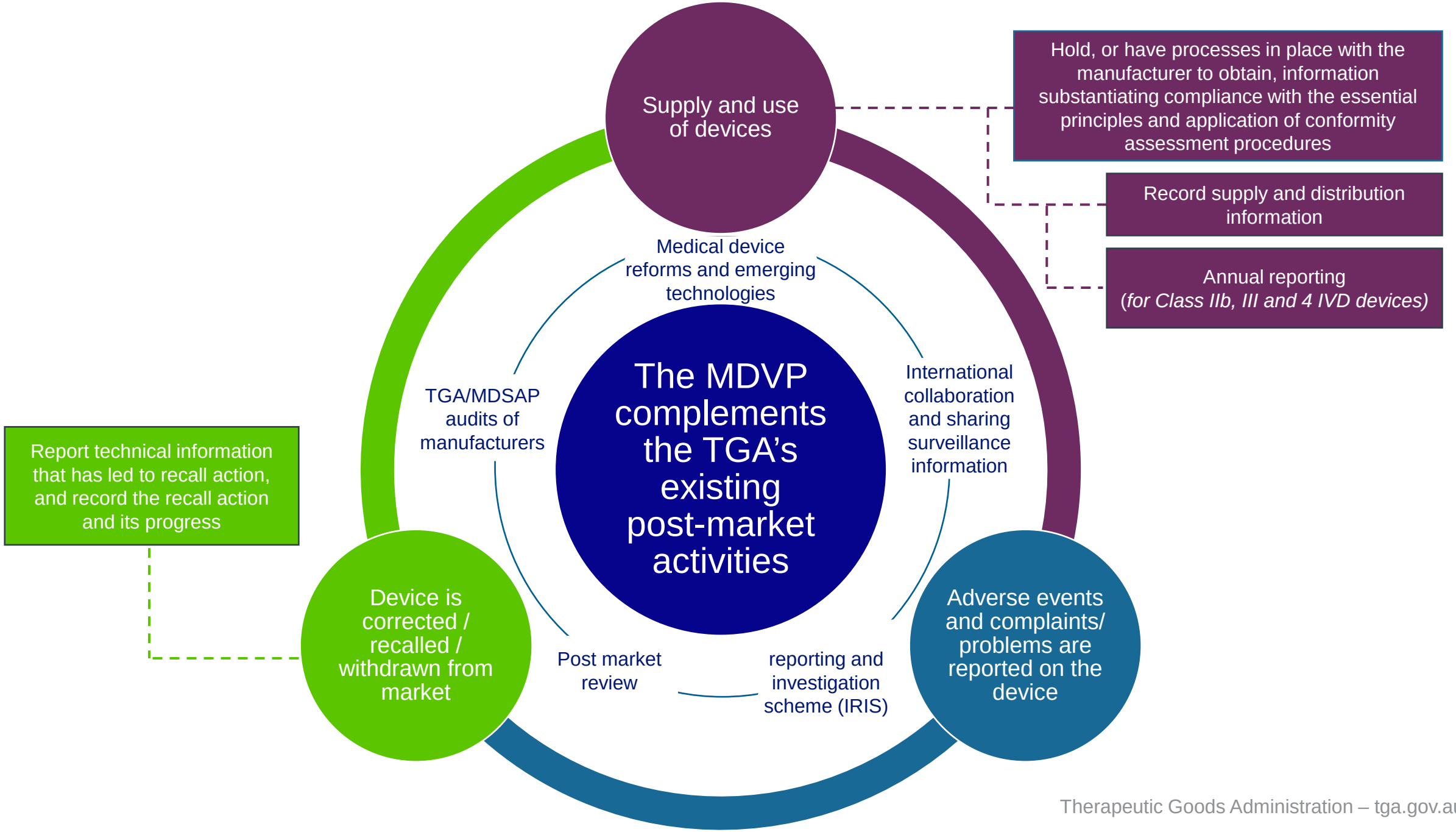
Increase access to, and availability and quality of the TGA's information that improves education, regulation and compliance



Improve the public's confidence in medical devices and its regulation

The MDVP aims to increase Australian medical device sponsors' understanding of, and compliance with, their post-market regulatory obligations.

It will complement the TGA's existing post-market monitoring, review and audit activities for medical devices.


Supply and use of devices
Hold, or have processes in place with the manufacturer to obtain, information substantiating compliance with the essential principles and application of conformity assessment procedures
Record supply and distribution information
Annual reporting (for Class IIb, III and 4 IVD devices)
Medical device reforms and emerging technologies
TGA/MDSAP audits of manufacturers
The MDVP complements the TGA's existing post-market activities
International collaboration and sharing surveillance information
Report technical information that has led to recall action, and record the recall action and its progress
Device is corrected / recalled / withdrawn from market
Post market review
reporting and investigation scheme (IRIS)
Adverse events and complaints/ problems are reported on the device

Regulatory requirements reviewed by the MDVP

Therapeutic Goods Act 1989

Sections 41FN, KA, MP/MPA

Therapeutic Goods (Medical Devices) Regulation 2002

Clauses 5.6-5.8, 5.10, 5.11, 8.1

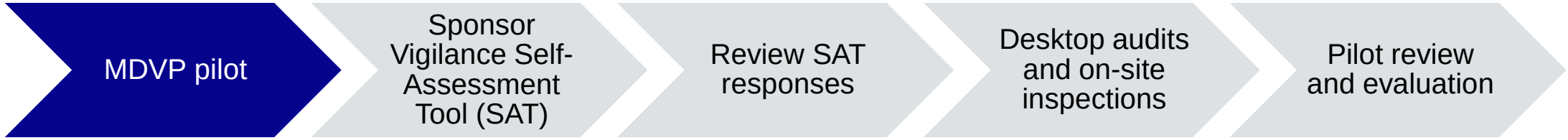
- Information substantiating compliance with EPs and CAPs
- Receive, record, relay and retain adverse event reports and complaints/problems
- Record and report recall actions and its progress
- Record supply and distribution information
- Annual reporting (*for Class IIb, III and 4 IVD devices*)

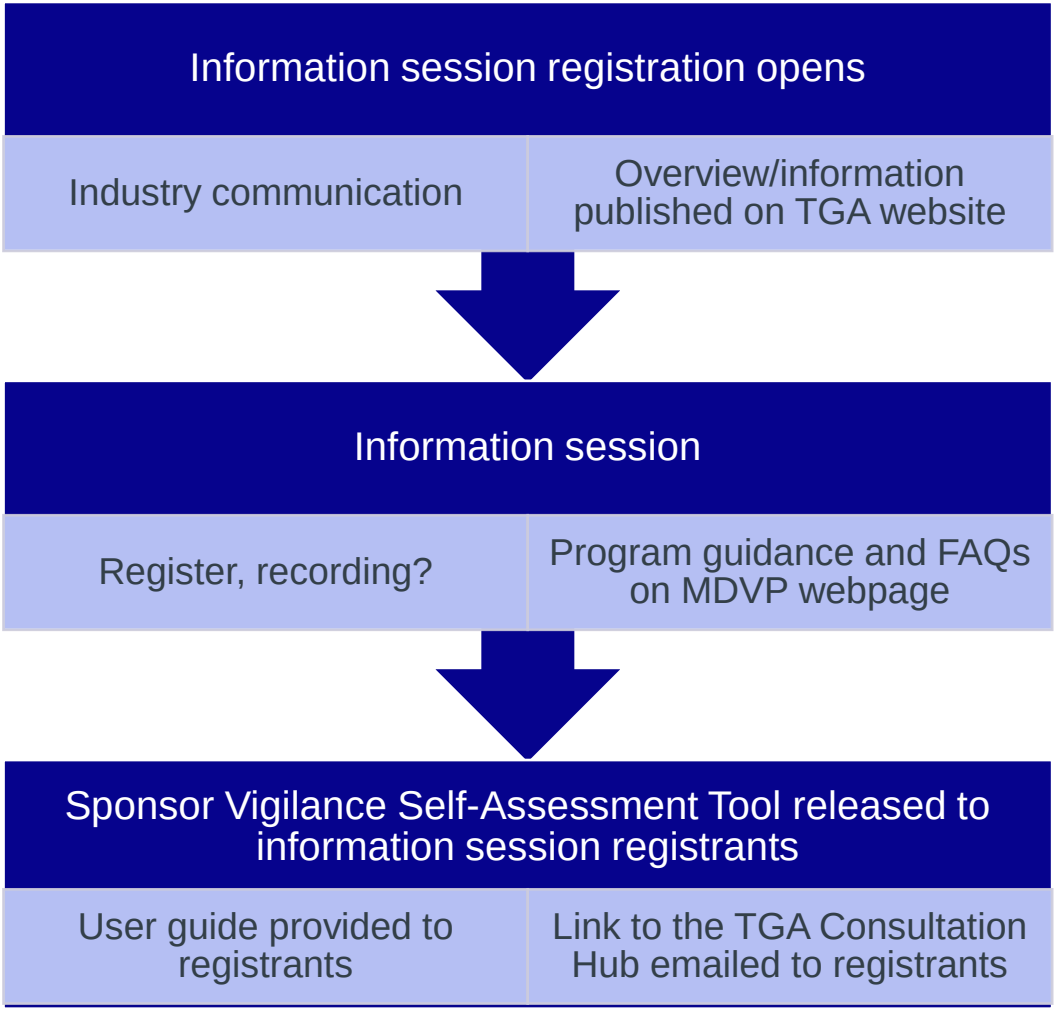
The MDVP pilot process

The MDVP pilot will run for 12 months across the 2023-24 financial year.

The pilot will:

- gather information from volunteer sponsors
- select sponsors to progress to the next stage, based on responses to the sponsor survey/SAT tool
- undertake desktop audits and on-site inspections, and
- identify areas for improvement



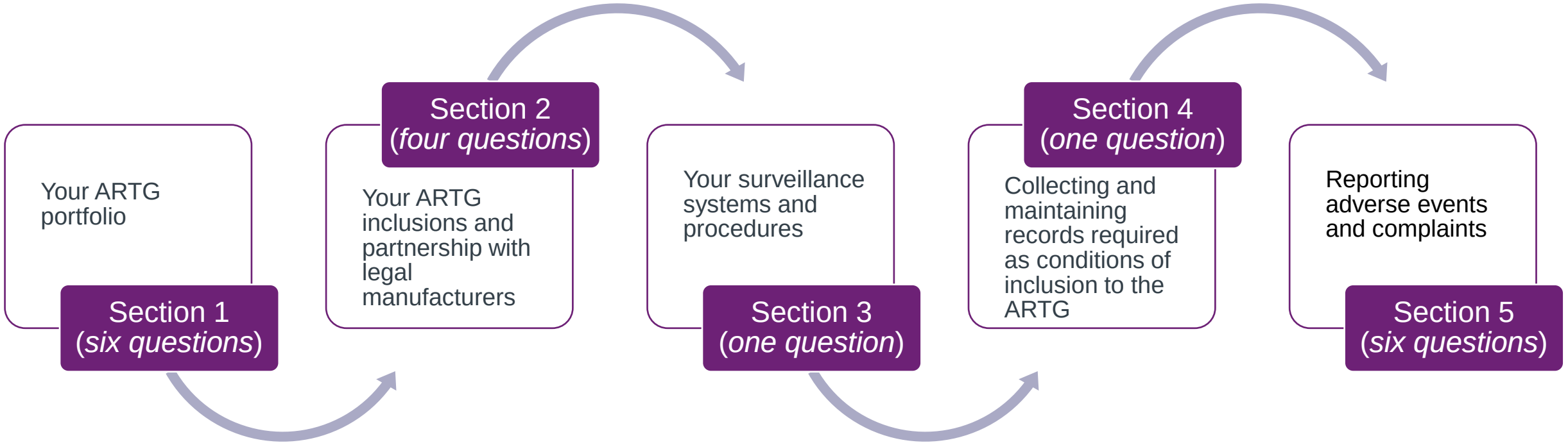


MDVP pilot commencement

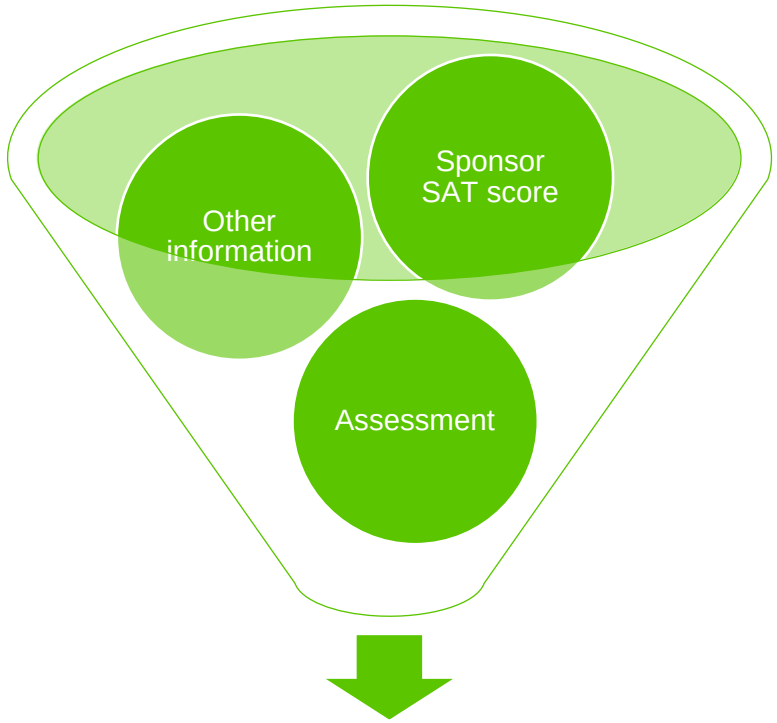
- **Register** and **attend** the information webinar to participate
- TGA MDVP webpage to support interested / volunteer sponsors
- Updates on the pilot will be through this webpage.

MDVP pilot | **Sponsor Vigilance Self-Assessment Tool (SAT)** | Review SAT responses | Desktop audits and on-site inspections | Pilot review and evaluation

Sponsor Vigilance Self-Assessment Tool



MDVP pilot | Sponsor Vigilance Self-Assessment Tool (SAT) | **Review SAT responses** | Desktop audits and on-site inspections | Pilot review and evaluation

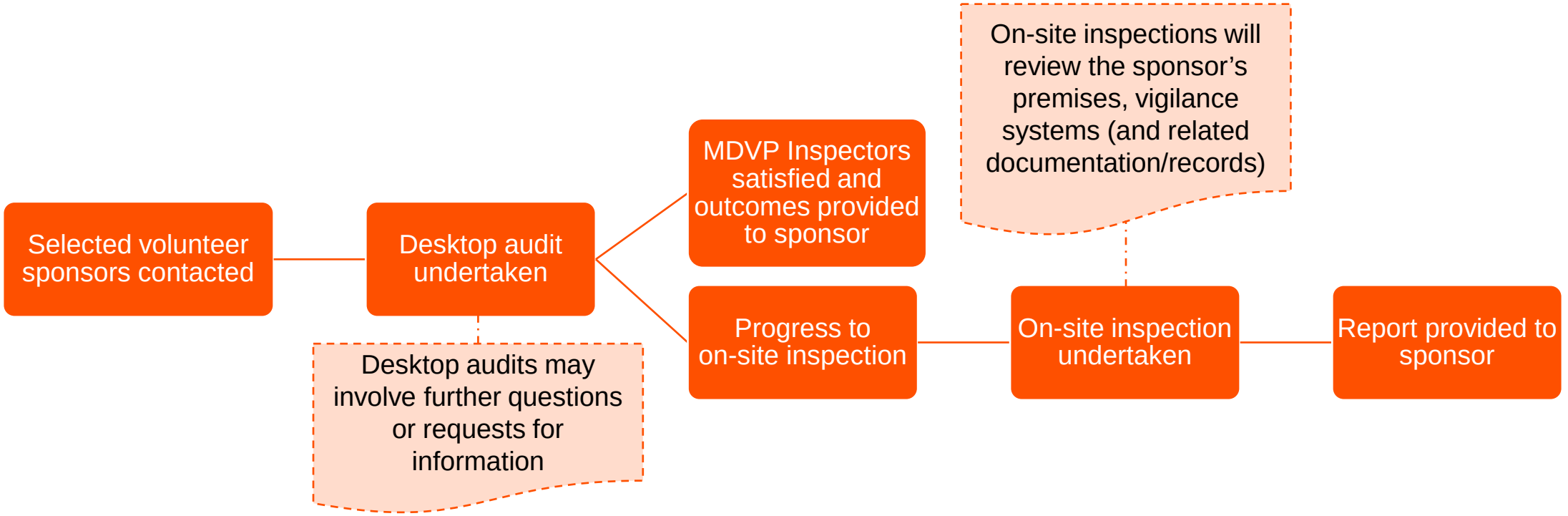


Review SAT responses

- Risk-based approach to select sponsors for desktop audits and/or on-site inspections
- Range of sponsors: i.e., different company sizes, experience, ARTG portfolio / device class diversity, etc can be selected

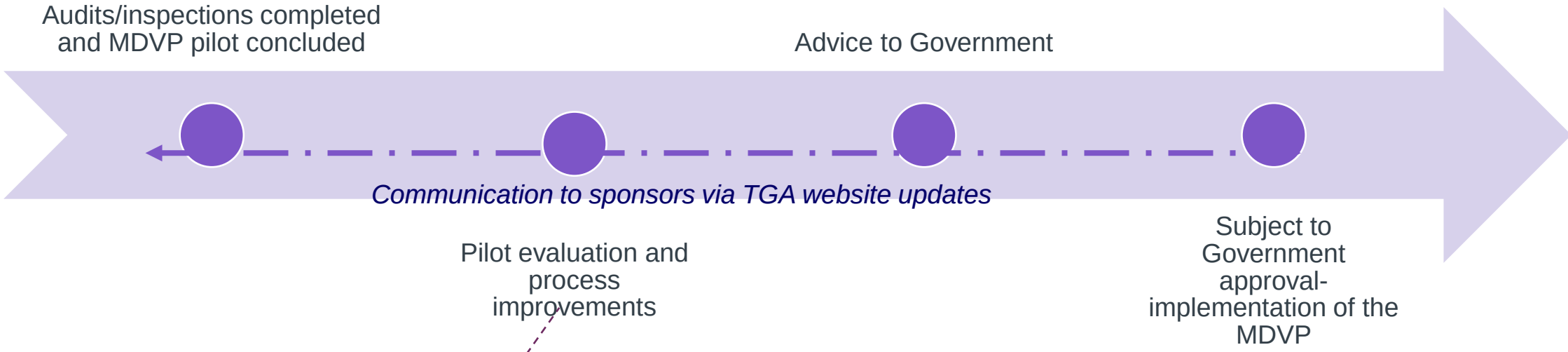
MDVP pilot | Sponsor Vigilance Self-Assessment Tool (SAT) | Review SAT responses | **Desktop audits and on-site inspections** | Pilot review and evaluation

Desktop audits and on-site inspections



MDVP pilot → Sponsor Vigilance Self-Assessment Tool (SAT) → Review SAT responses → Desktop audits and on-site inspections → **Pilot review and evaluation**

Pilot review and evaluation



Touchpoints for sponsor feedback:

- After information session (and associated education sessions)
- SAT user experience questionnaire (following SAT completion)
- [*if sponsor is selected for audit/inspection*] Following audit/inspection process
- Ongoing opportunity for feedback through the MDVP webpage and emails

Next steps and what to look out for

- Government approval to commence the MDVP pilot
- Communication from the TGA on the information session
- MDVP website
  Information session registration
- Contact us: MDVP@health.gov.au.

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