How to Manage GMP Compliance Signals:

For Sponsors and Manufacturers of Medicines and Biologicals

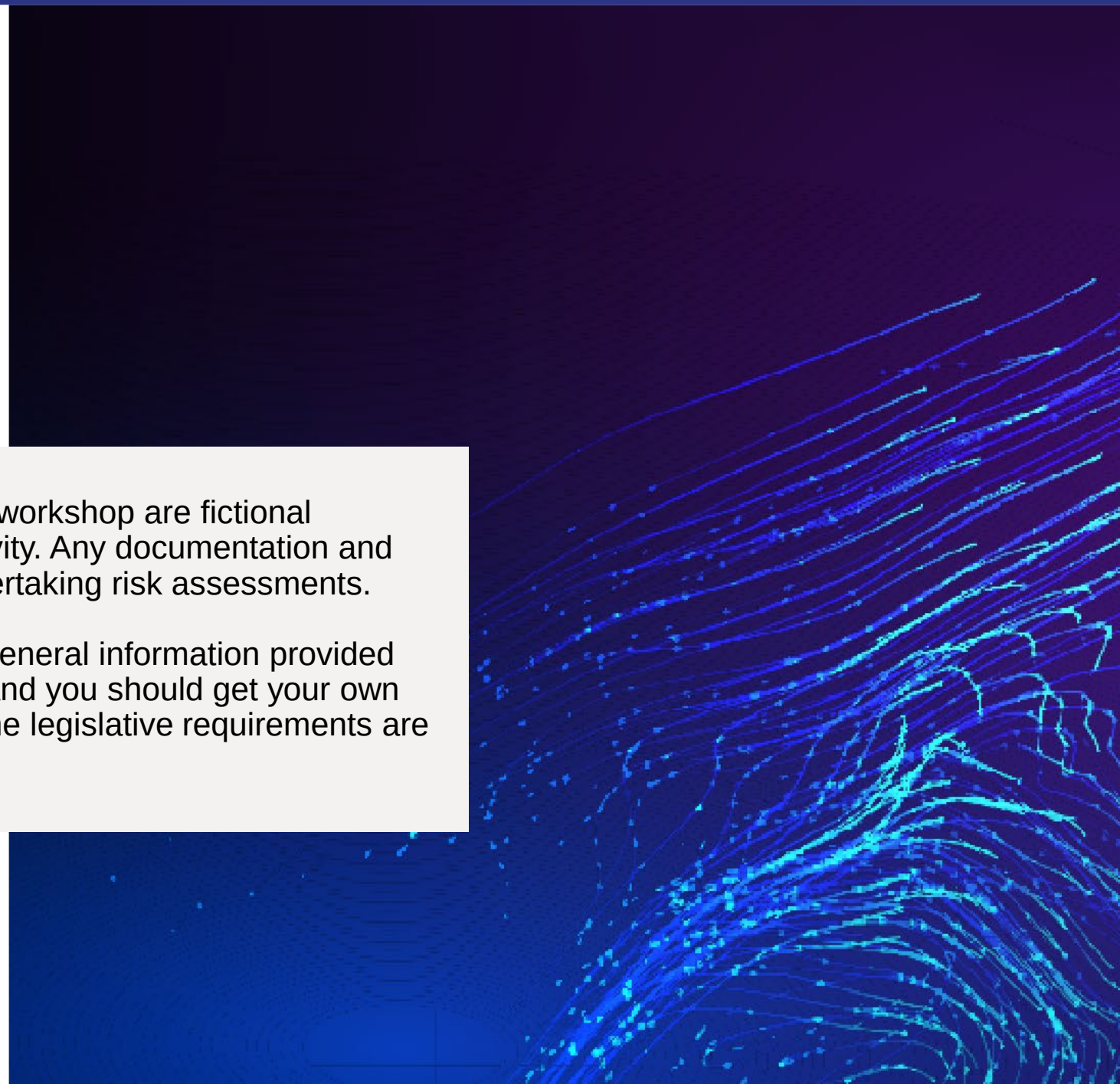
GMP Signals Investigation and Enforcement team
Manufacturing Quality Branch
Department of Health and Aged Care, TGA

GMP FORUM 2024

Disclaimer

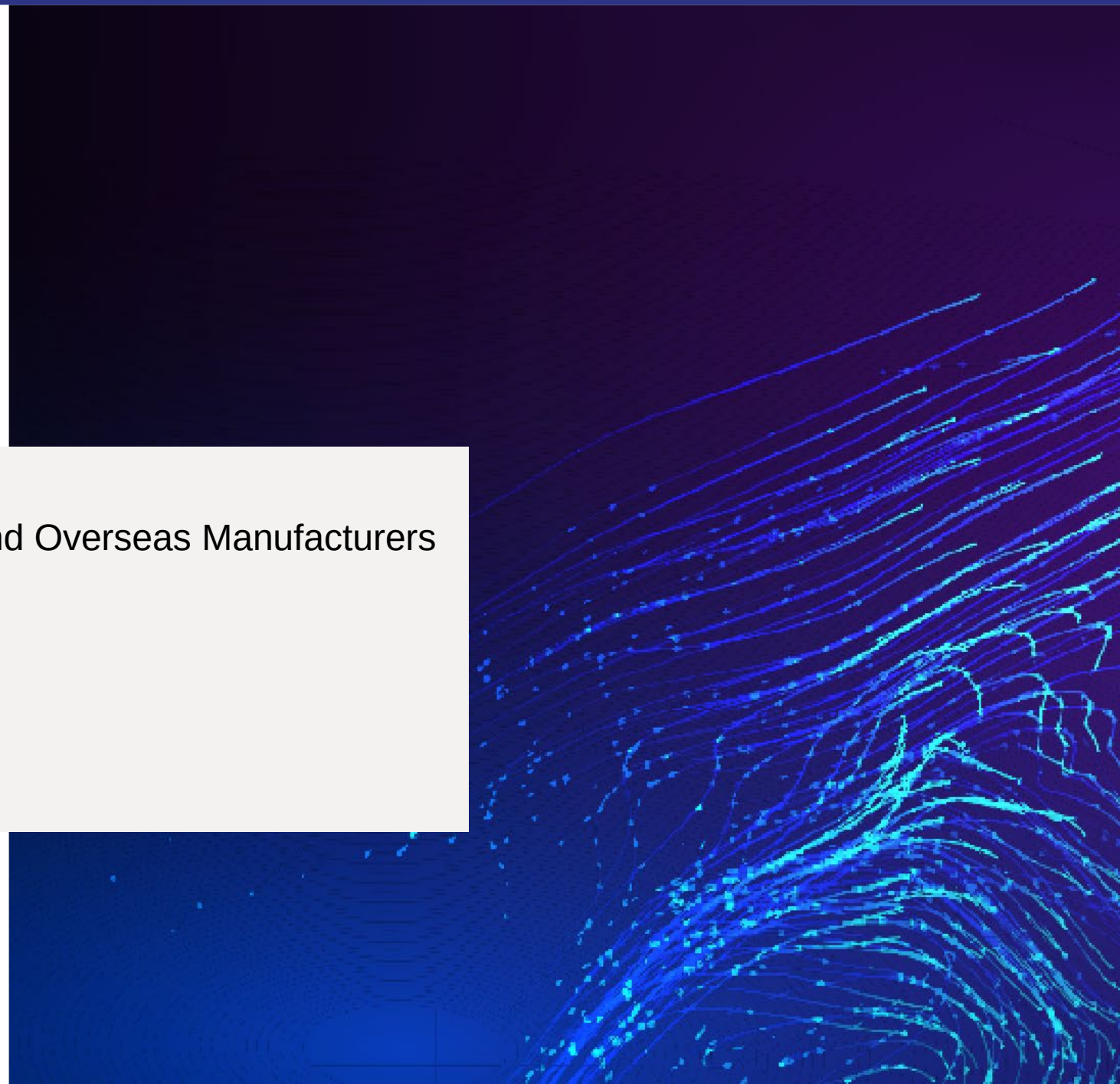
The information and scenarios provided in this workshop are fictional examples only to assist with the workshop activity. Any documentation and outcomes should not be relied upon when undertaking risk assessments.

The information contained in this workshop is general information provided without prejudice; it is not binding on the TGA and you should get your own independent legal advice to ensure that all of the legislative requirements are met.



Agenda

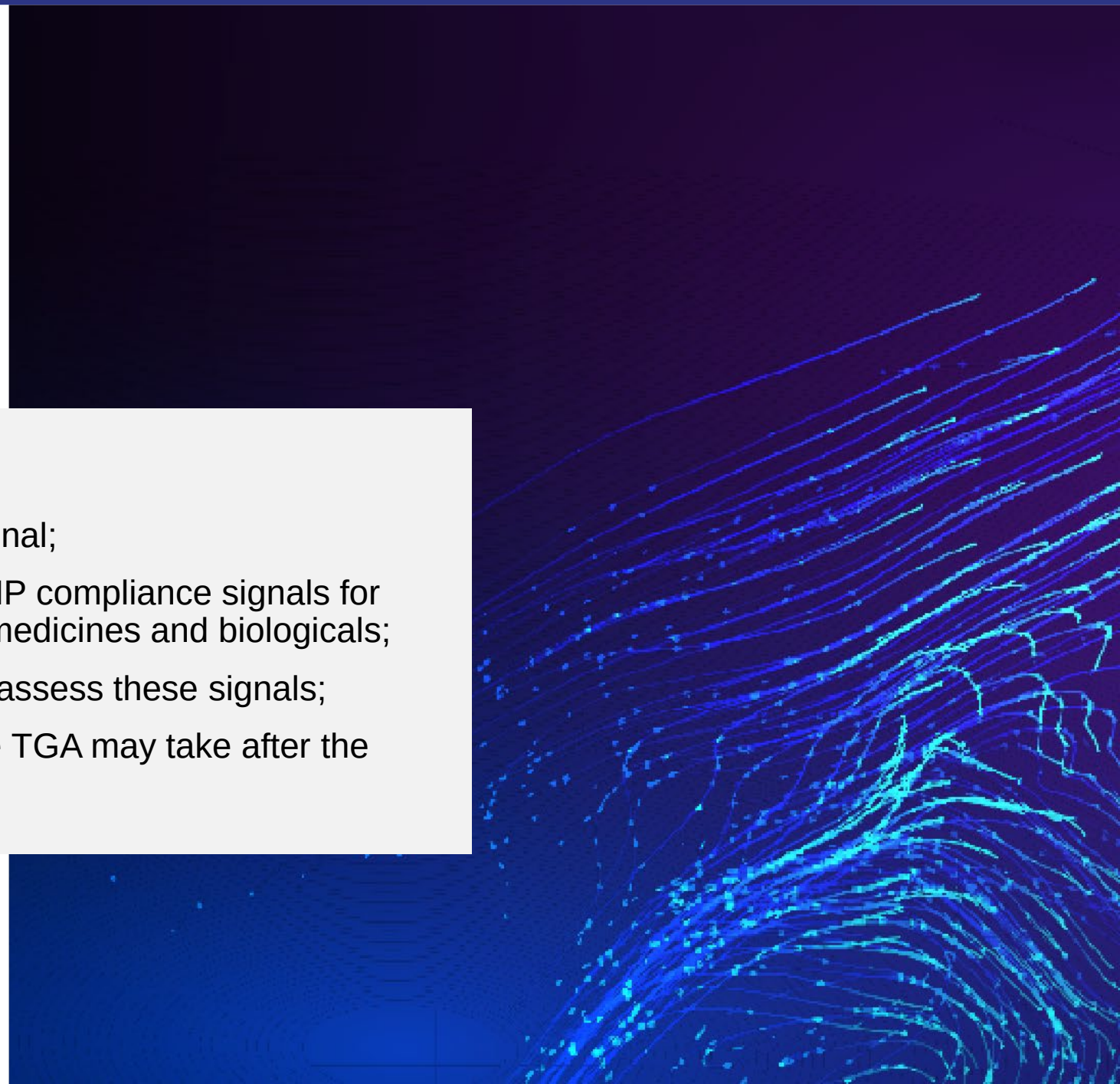
- Presentation - GMP Signal Overview and Overseas Manufacturers
- Workshop Activity
- Presentation – Domestic Manufacturers
- Questions



Learning outcomes

This session provides learning opportunities:

- Understand what is a GMP compliance signal;
- Understand the TGA's management of GMP compliance signals for domestic and overseas manufacturers of medicines and biologicals;
- What information the TGA may request to assess these signals;
- The regulatory and enforcement action the TGA may take after the assessment of GMP compliance signals.



Who are we and what do we do?

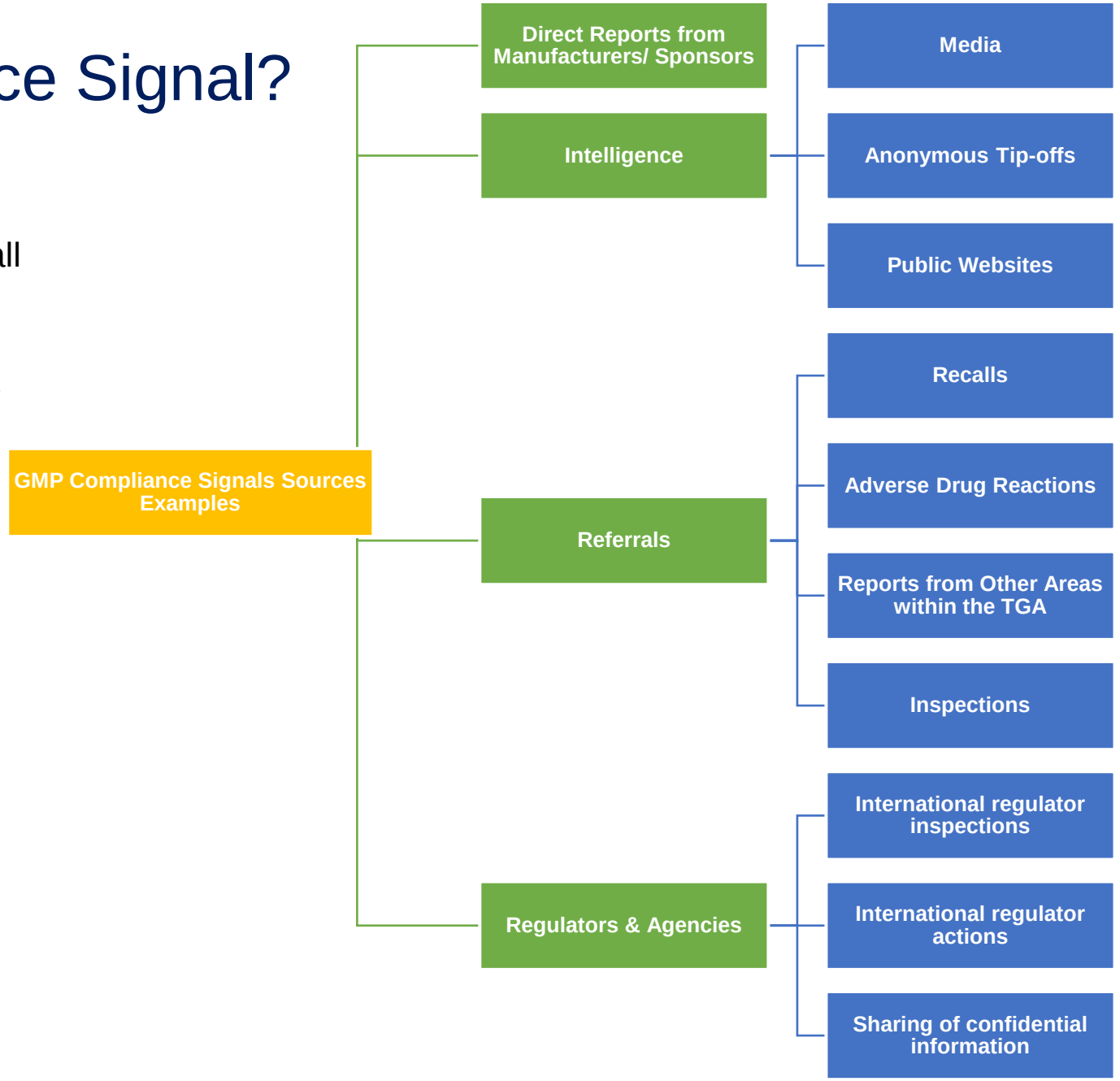
GMP Signals Investigation and Enforcement team

We are responsible for:

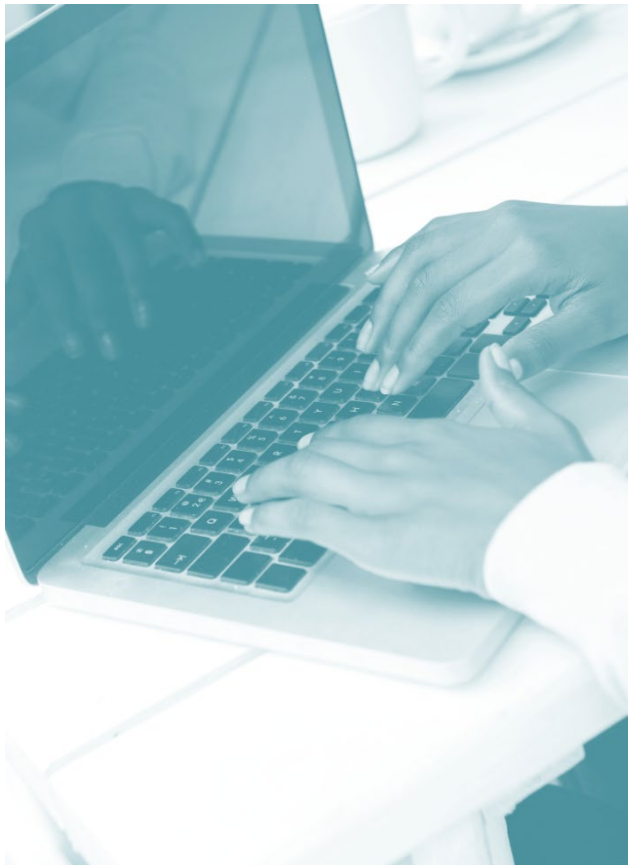
- Investigating non-compliance alerts to ensure products meet quality requirements. This includes information from TGA inspections and the regulatory actions of other regulators.
- Investigating potential manufacturing breaches following reports from the public to the TGA (for example, whistleblower reports or adverse event reports).
- Recommending regulatory and enforcement action where breaches of the PIC/S code of GMP or the *Therapeutic Goods Act 1989* have occurred.

What is a GMP Compliance Signal?

- For medicinal products supplied in Australia, all steps of manufacture must be compliant with GMP unless they are exempt.
- GMP Compliance signals are non-compliance alerts that include intelligence, data and information that we receive from numerous sources that indicate a departure from the manufacturing principles (or equivalent overseas standard) by a manufacturer.
- Sources of GMP Signals may be internal or external.



Reporting a GMP Compliance Signal



Who can report a GMP Compliance Signal?

Anyone can report a GMP Compliance Signal.

It is expected that sponsors and manufacturers report GMP Compliance signals to the TGA when they become aware of such information.

How to report a GMP Compliance Signal?

Reports can be made anonymously via Report a breach | Therapeutic Goods Administration (TGA) page on the TGA website.

Alternatively, you can report directly to the GMP Signals Investigation and Enforcement Team by emailing GMPCompliance@health.gov.au or calling 1800 020 653.

Quiz – What should be reported to the TGA?

Which of the following items should be reported to the TGA as a potential or actual GMP Compliance Signal?

US FDA Warning Letter
US FDA 483 Form
Acceptable Overseas Inspection Outcome
US FDA Import Alert
TGA Licence Breaches
EUDRA Statement of Non-compliance with GMP
Unacceptable Overseas Inspection Outcome
Damage to Manufacturing Facilities
Media Reports

Quiz Answers – What should be reported to the TGA?

Which of the following items should be reported to the TGA as a potential or actual GMP Compliance Signal?

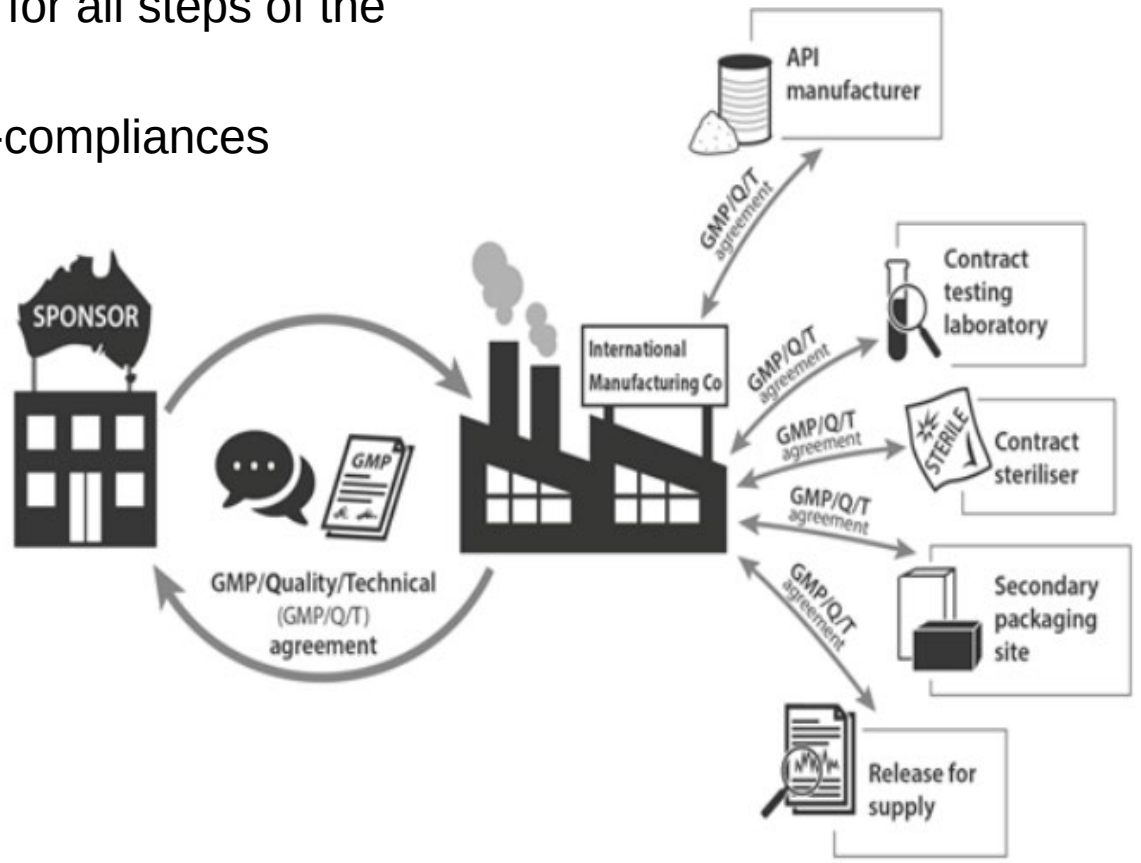
Item	Answer
US FDA Warning Letter	Yes
US FDA 483 Form	No
Acceptable Overseas Inspection Outcome	No
US FDA Import Alert	Yes
TGA Licence Breaches	Yes
EUDRA Statement of Non-compliance with GMP	Yes
Unacceptable Overseas Inspection Outcome	Yes
Damage to Manufacturing Facilities	Yes
Media Reports	No

Supply Chains

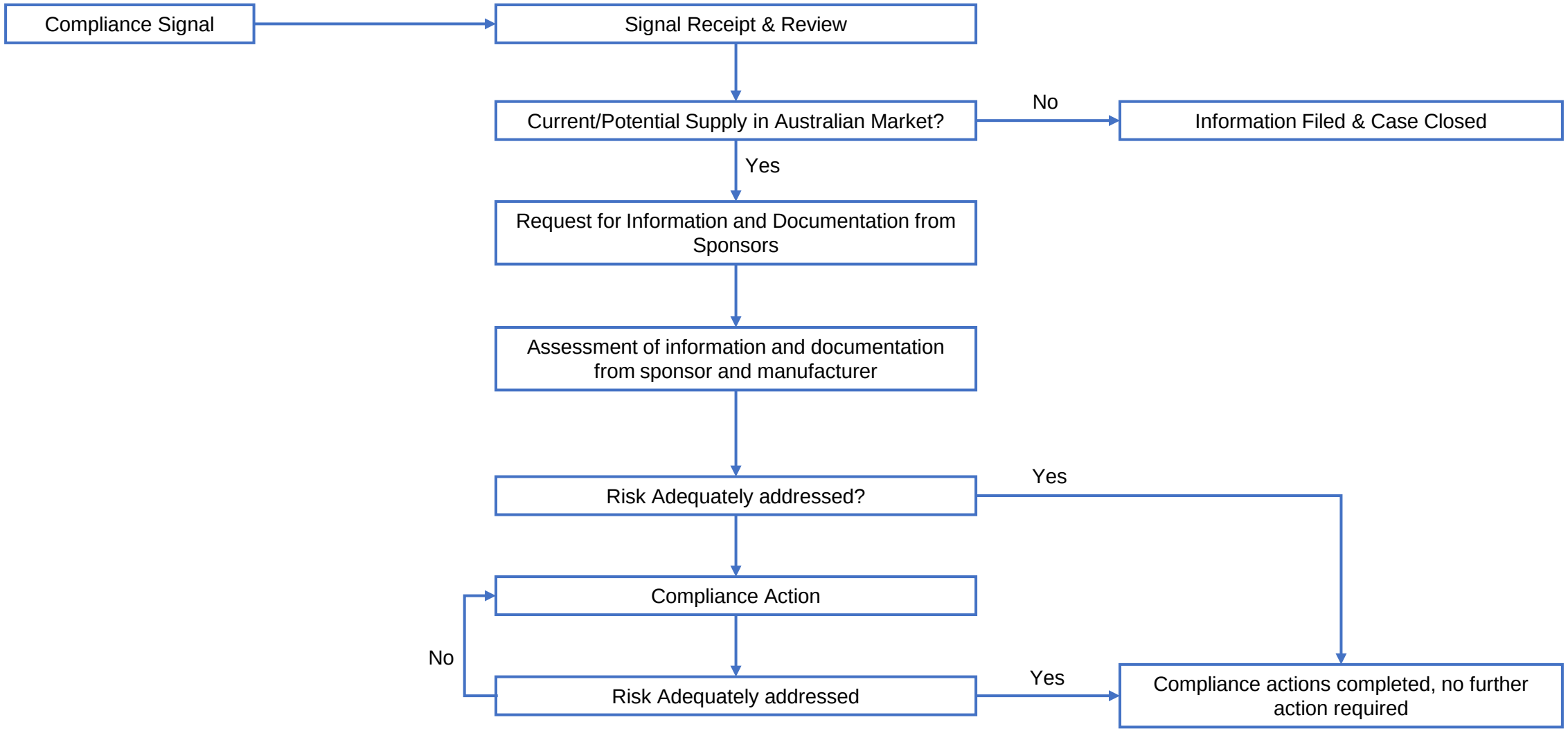
Sponsors should have awareness of their supply chain.

Sponsors should

- Ensure an appropriate quality agreement in place for all steps of the supply chain
- Establish communication around reporting of non-compliances with all the parties from the supply chain.
- Understand the roles and responsibilities of each site and their involvement in your product manufacturing process
- Ensure appropriate actions taken in line with the quality agreement in place.
- Notify the TGA of when you are aware of a non-compliance.



GMP Compliance Signals Process – Overseas Manufacturer



Example: Overseas Unacceptable Inspection Outcome

You've received an email from GMP Compliance – What does this mean? What information do I need to provide?

Part 1 – Details of Product Supply Information Relating to the Manufacturer

- List of products supplied to Australia
- Issued GMP Clearances
- GMP Clearance and Product Applications

Part 2 – Product Risk Assessment

- Manufacturer site response and risk assessments
- Sponsor risk assessments related to your products

Further information may be requested by the TGA.

Example: Overseas Unacceptable Inspection Outcome

You've provided information to the TGA – What happens next?

- GMP Clearance applications will be placed on hold.
- All information provided will be reviewed and assessed.
- Consultation with internal TGA subject matter experts (if required).
- The TGA will make an unbiased decision based on the information provided by sponsors.
- If sponsors chose not to provide information/ risk assessments, the TGA is unable to make an assessment and may take action on GMP clearances.
- Sponsors will be notified of the investigation outcome and any compliance actions.

Example: Overseas Unacceptable Inspection Outcome

What happens when risks are not adequately addressed?

- Regulatory action taken will be based on risk and on a case-by-case basis.

- Where it is deemed that there are risks the following action may be taken
    - Product recall action
    - TGA Compliance inspection
    - Action on GMP Clearance(s)
    - Suspension/ Cancellation of ARTG(s)

Risk Assessments

What is important?

- Risk assessments should be prepared in accordance with PIC/S GMP Guide Annex 20 / ICH9 Quality Risk Management
- The risk assessment must
    - (1) Address the deficiencies cited in the non-conformance report and;
    - (2) Identify the root cause where applicable and outlines risk assessment, evaluation, rationale, corrective and preventative actions and/or risk mitigating strategies to support the continued supply of products from this site to Australia.

- Risk assessments should be conducted by both the sponsor and manufacturer. Submitting a manufacturers risk assessment on its own insufficient.
- Sponsor risk assessments scope should include all products supplied to Australia and include a review of the manufacturers CAPA to address the GMP deficiencies.

Workshop Activity – Case Study

You have been split into two groups: non-sterile and sterile.

On the table you have the following:

- Workshop booklet containing 2 scenarios
- Butchers paper to write your responses

Scenario

You are a sponsor, and a manufacturer in your supply chain received a GMP non-conformance report.

In your groups, review and discuss the non-conformance report. Your response should identify which deficiencies impact your products. On the butcher’s paper add your answers to the questions for each scenario.

Domestic Manufacturing Sites

GMP Signal investigation

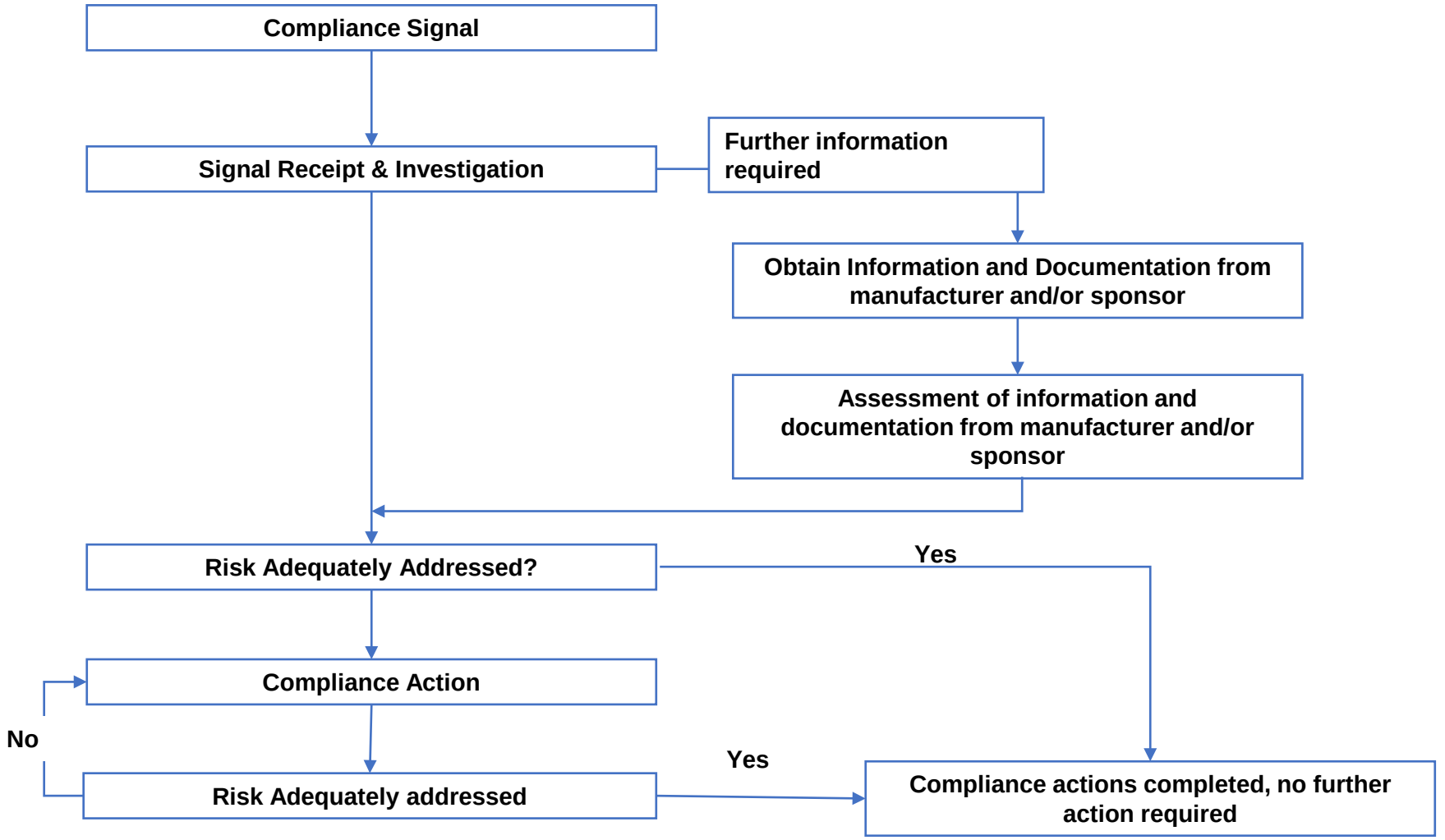
TGA inspections assess the GMP compliance of your site.
The TGA may take actions at any stage of the inspection process on a case-by-case basis.

The TGA receives whistleblower reports and tip off that are investigated.

Compliance actions may be considered if:

- Recurring deficiencies are not addressed
- Critical deficiencies are identified
- A licence breach is identified
- Product risks are identified

GMP Compliance Signals Process – Domestic Manufacturer

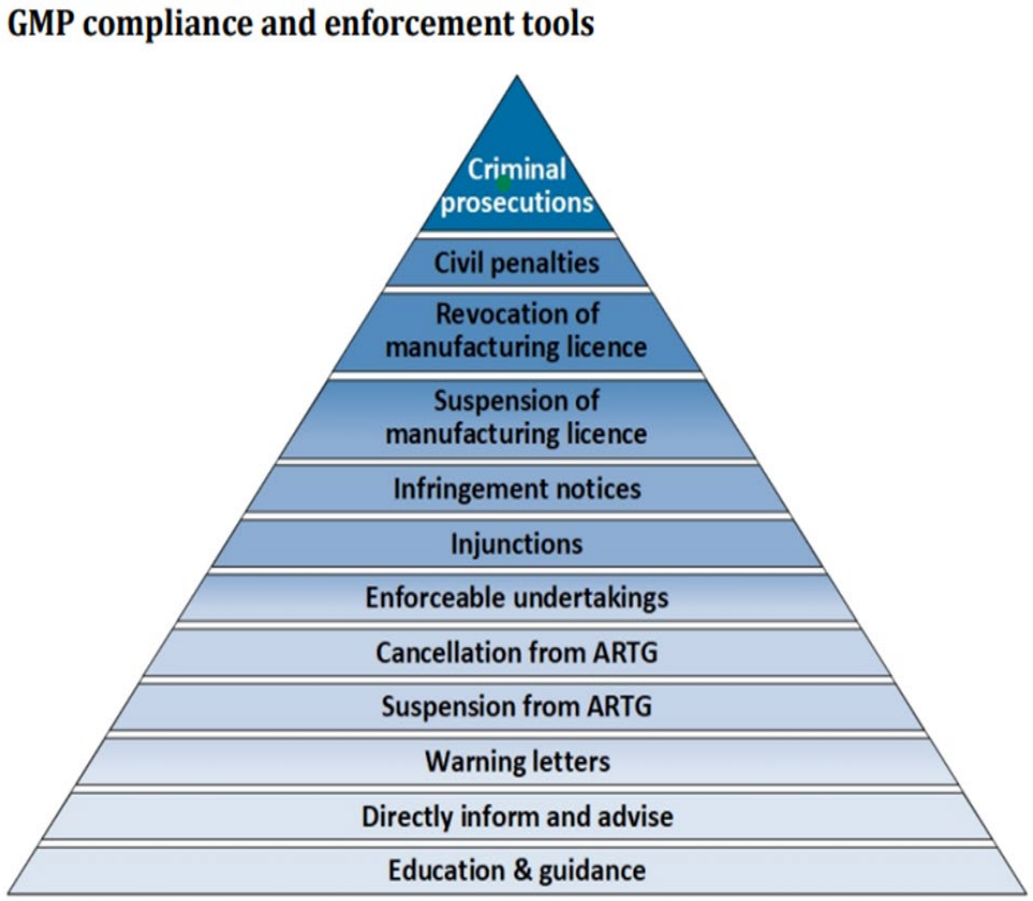


Compliance and Enforcement Actions for Domestic Manufacturers

Escalation of Compliance Actions

The TGA have a range of tools available to use where there is a demonstrated breach of the *Therapeutic Goods Act 1989, Regulations* or the manufacturing principles.

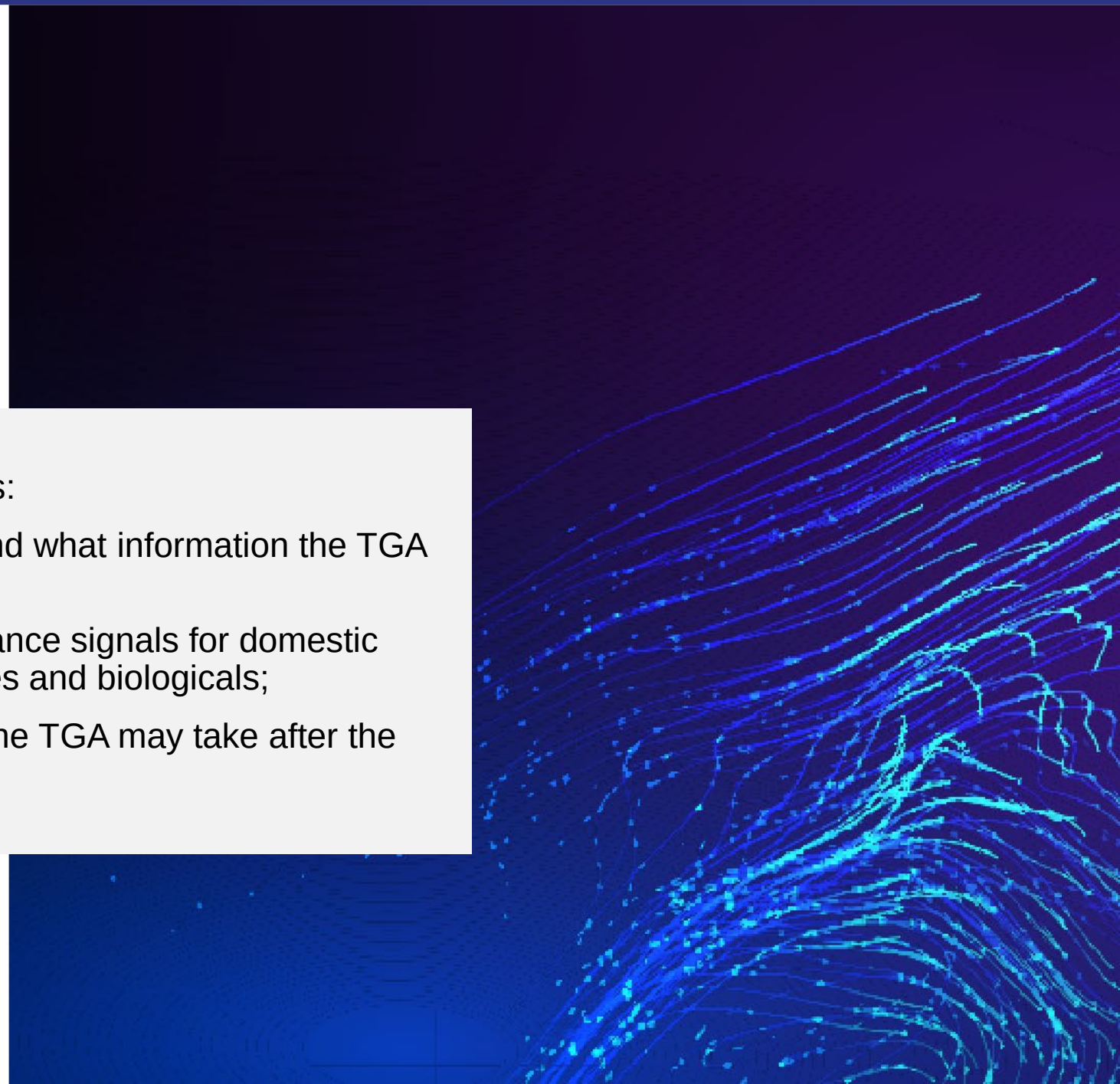
- The compliance triangle is not a ladder. We can take any action that is consummate to the potential risks for products or consumers.
- Actions taken in the last year include licence revocation, recalls, warning letters and infringement notices.



Summary

This session provided learning opportunities:

- Overview of GMP Compliance signals and what information the TGA may request to assess these signals;
- The TGA's management of GMP compliance signals for domestic and overseas manufacturers of medicines and biologicals;
- The regulatory and enforcement action the TGA may take after the assessment of GMP compliance signals.



Questions?

Scan the QR code with your device to submit a question

GMP FORUM 2024

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration