Release for Supply (Batch Certification) – Meeting Your Obligations as an Authorised Person

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GMP FORUM 2024

Agenda

- What is Annex 16
- Authorised Person requirement
- Purpose of Batch release
- New terms
- Information for the Authorised Person
- Confirmation Declaration
- Release for supply (batch certification)
- Myths
- Common deficiencies
- Scenario

What is Annex 16?

Overview

- Annex 16 is a new annex in the PIC/S Guide to GMP
- Provides clear guidance for Authorised Persons in performing Batch Certification or Release for Supply.
- It has been developed based on the EU GMP Annex 16.

What is Annex 16?

What does it apply to?

This Annex applies to the certification of goods

Applies to the assessment of medicinal products and their intermediate stages for confirmation of compliance with:

- GMP;
- the Marketing Authorisation (MA);
- Clinical Trial Authorisation, (CTA);
- and any other relevant regulations

What is Annex 16?

What did we have before Annex 16?

The preceding versions of the PIC/S Guide contained only basic information regarding batch certification

Release for Supply guidance and Guidance for Releasing medicines manufactured at multiple sites.

What is Annex 16?

Holistic approach

Release for supply captures

- All relevant elements of the pharmaceutical quality system (PQS)
- Relevant annexes
- Relevant guidance published

What is Annex 16?

Scope clarification

Mandatory Import testing

- Only if in the marketing authorisation
- If testing, then sampling plans must be justified

Import parallel testing of goods

- Not permitted under the Australian regulatory framework.
- Clause is not applicable

Authorised Person requirement

Definition

An authorised person is a person recognised by the authority as having the necessary basic scientific and technical background and experience. Authorities identify who the authorised persons are through the manufacturer's pharmaceutical quality system.

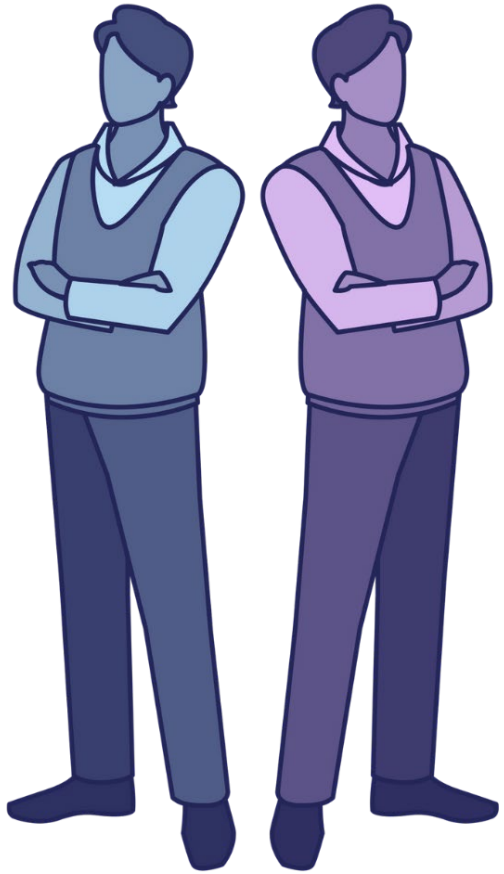
Authorised person(s): an employee or employees authorised by a TGA approved manufacturer through a statement in the manufacturer's pharmaceutical quality system to perform release for supply.

The person nominated to have control of quality control under section 37(1)(e), *Therapeutic Goods Act 1989* would be an obvious choice to be an authorised person, but other arrangements can be considered, including delegation.

Authorised Person requirement

Authorised Person vs QP

- The references within Annex 16 to “Authorised Persons” (AP) is consistent with existing terminology used within the PIC/S GMP guide
- There is no change to the existing framework for Authorised Persons.



- The EU GMP Annex 16 refers to the use of Qualified Persons (QP), defined within EU Directive 2001/83/EC
- The TGA **does not** intend to adopt a QP framework for Authorised Persons, and existing expectations for Authorised Persons will remain without amendment.

Authorised person requirement

Related clauses in PIC/S guide

Principle

There are additional legal responsibilities for the holder of the Manufacturing Authorisation and for the Authorised Person(s).

Clause 1.4 xv

Medicinal products are not sold or supplied before an Authorised Person has certified that each production batch has been produced and controlled in accordance with the requirements of the Marketing Authorisation and any other regulations relevant to the production, control and release of medicinal products;

Authorised person requirement

Related clauses in PIC/S guide

Clause 1.9 vii

No batch of product is released for sale or supply prior to certification by an Authorised Person that it is in accordance with the requirements of the relevant authorisations;

Clause 2.2

The manufacturer must have an organisation chart in which the relationships between the heads of Production, Quality Control and where applicable Head of Quality Assurance or Quality Unit referred to in point 2.5 and the position of the Authorised Person(s) are clearly shown in the managerial hierarchy.

Authorised person requirement

Related clauses in PIC/S guide

Clause 2.6

The duties of the Authorised Person(s) are described in the national requirements and can be summarised as follows:

a) An Authorised Person must ensure that each batch of medicinal products has been manufactured and checked in compliance with the laws in force in that country and in accordance with the requirements of the Marketing Authorisation;

b) The Authorised Person(s) must meet the qualification requirements laid down in the national legislation, they shall be permanently and continuously at the disposal of the holder of the Manufacturing Authorisation to carry out their responsibilities;

c) The responsibilities of an Authorised Person may be delegated, but only to other Authorised Person(s).

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Authorised person requirement

Training and experience - Expectations

Level of education and expertise = steps of responsibility

Proficient in the release for supply requirements of the PQS

Appropriate knowledge for the specific steps in manufacture for which responsibility is taken

Keep knowledge up-to-date in light of:

- technical and scientific progress
- changes in quality management relevant to the release that they authorise

Purpose of batch release

What am I signing up for?

Each batch has been produced and controlled in accordance with all the requirements of any marketing authorisations (or equivalent) or including:

- any other regulations relevant to the production, control and release of the therapeutic good manufactured under GMP
- Meet GMP requirements
- Manufacturing authorisations are in place
- At least one AP
- GMP agreements
- Release testing processes
- all necessary steps have been completed in accordance with the pharmaceutical quality system (PQS), regardless of how many sites are involved

Confirmation

Certification

New terms

Confirmation vs Certification

Confirmation = Release for further processing (RFFP)

Certification = Release for supply (RFS)

Quiz

What sector do you represent:

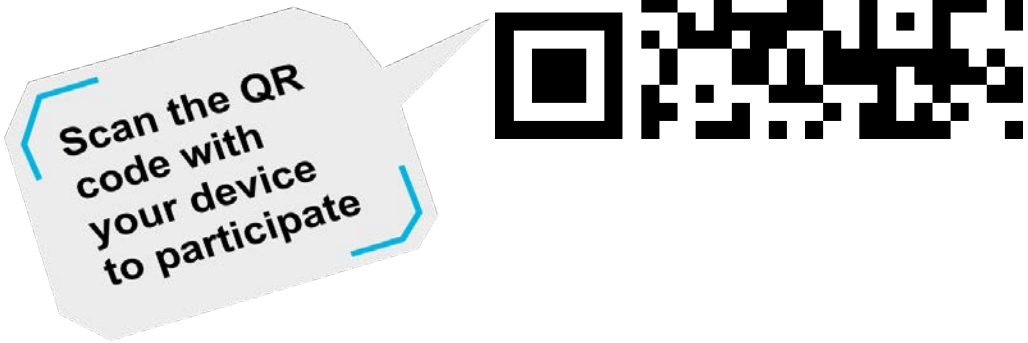
- ❑ Listed Medicines
- ❑ Registered Medicines
- ❑ Medicinal Cannabis
- ❑ Investigational Medicinal products
- ❑ Blood
- ❑ Biologicals
- ❑ Compounding
- ❑ Radiopharmaceuticals
- ❑ Other

Scan the QR code with your device to participate in this activity

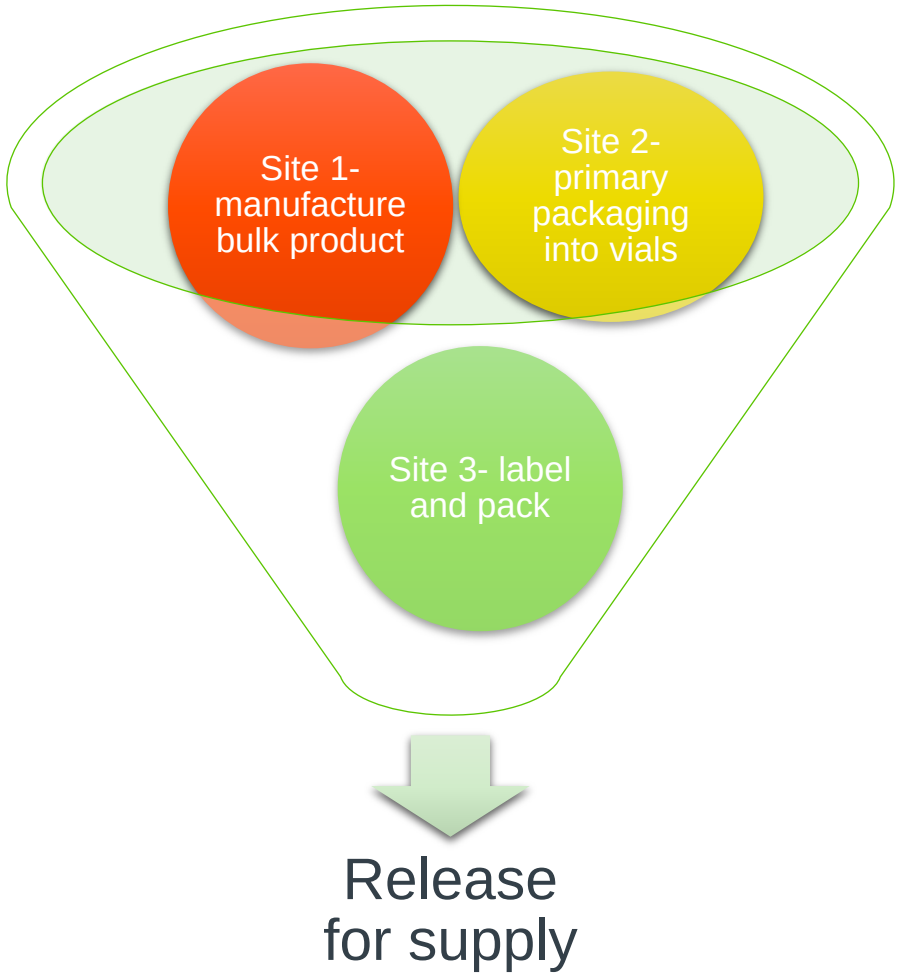
Quiz

Are there areas that you are not sure about? (Can include more than one area):

- ❑ Authorised person requirements
- ❑ Confidentiality
- ❑ Access to information
- ❑ Supply chains
- ❑ Audits
- ❑ PQRs
- ❑ Ongoing stability
- ❑ GMP agreements
- ❑ Declarations for Confirmation
- ❑ Declarations for Certification



Partial manufacture

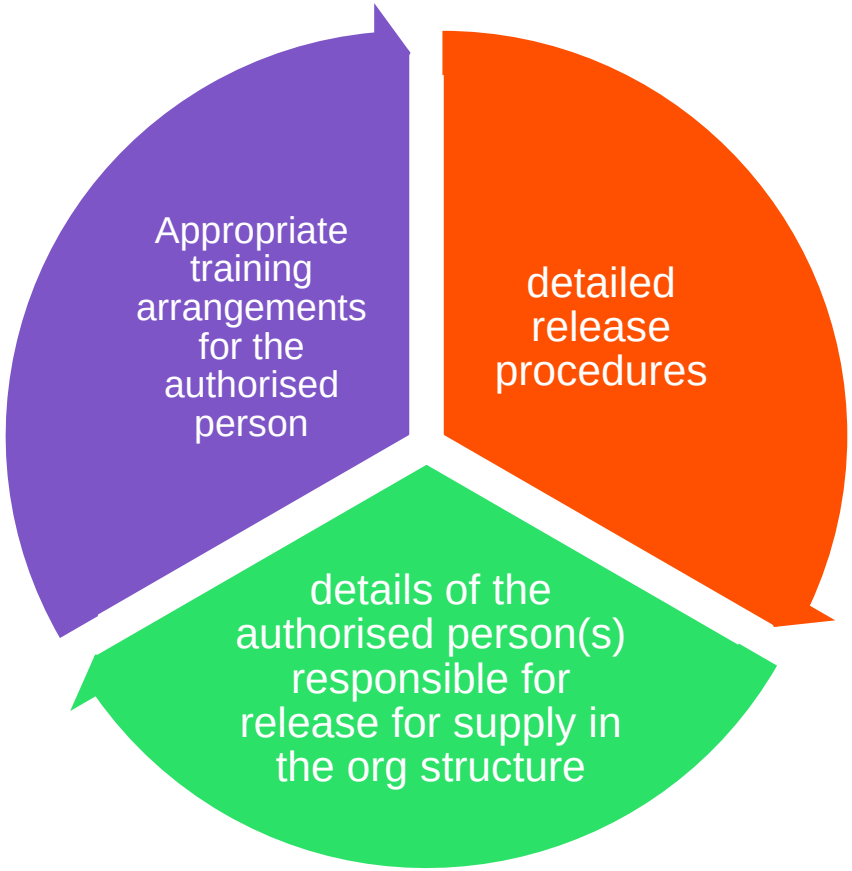


Partial Manufacture

Pharmaceutical quality system elements

Partial Manufacture

Pharmaceutical quality system elements



Authorised person performing certification

Access to information

The AP makes decisions for certification based on information from partial manufacturers:

- ✓ Signed confirmation declaration
- ✓ Marketing and manufacturing authorisations or equivalent
- ✓ Certificate of Analysis
- ✓ Ongoing stability data, PQRs, audits

Information for the Authorised Person

Confidentiality

Approach

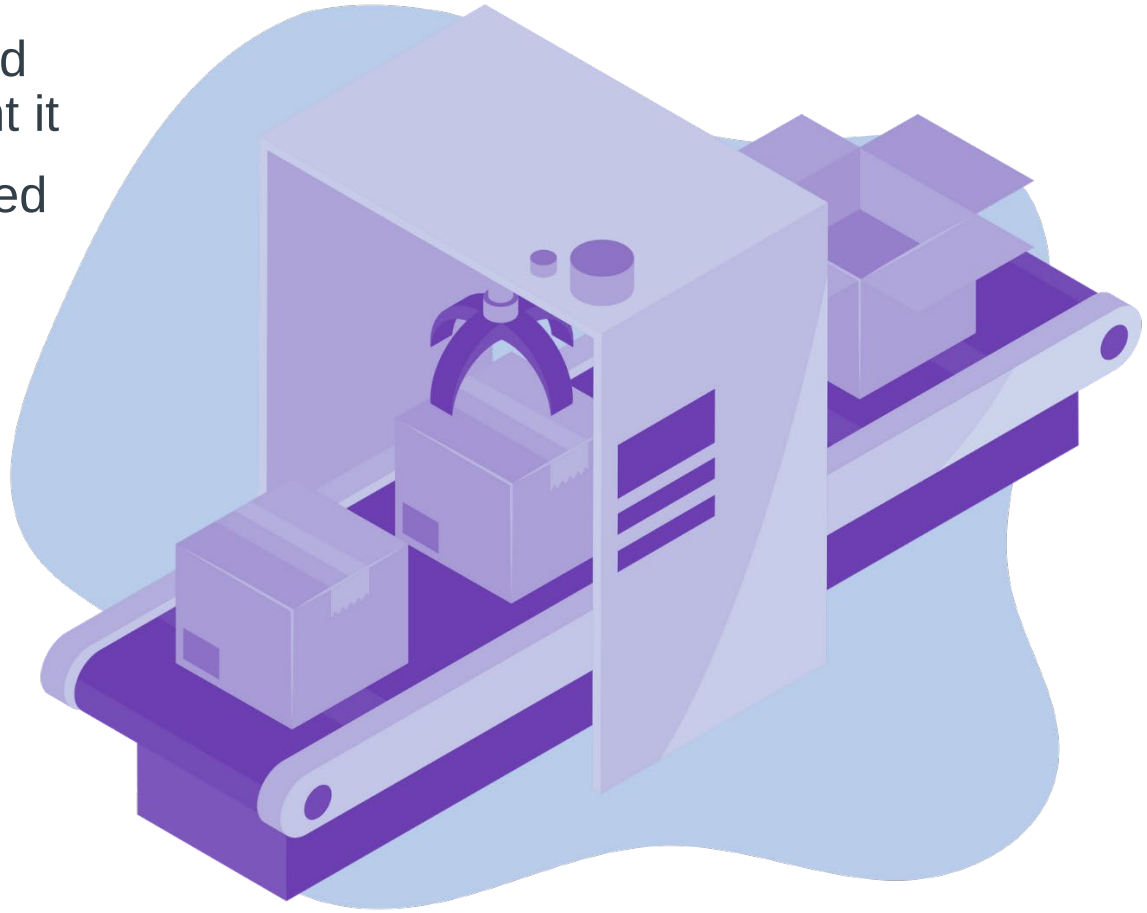
If you are concerned about confidentiality:

- Sign a confidentiality agreement
- Obtain a TGA licence to perform RFS
- Mechanism for access to information to the AP direct
- Explore manufacturer who performs RFS
- Look at your GMP agreement

Information for the Authorised person

Supply chain principles

- Know the supply chain of the active substance and medicinal product up to certification and document it
- In the format of a comprehensive diagram preferred
- Includes each party, subcontractors of critical steps



Information for the Authorised Person

GMP agreement requirements

Sponsors and manufacturers are required to establish valid GMP agreements to cover all partial manufacturers in the supply chain in accordance with the PIC/S Guide to GMP

- ✓ Responsibilities
- ✓ Communication channels

Information for the Authorised Person

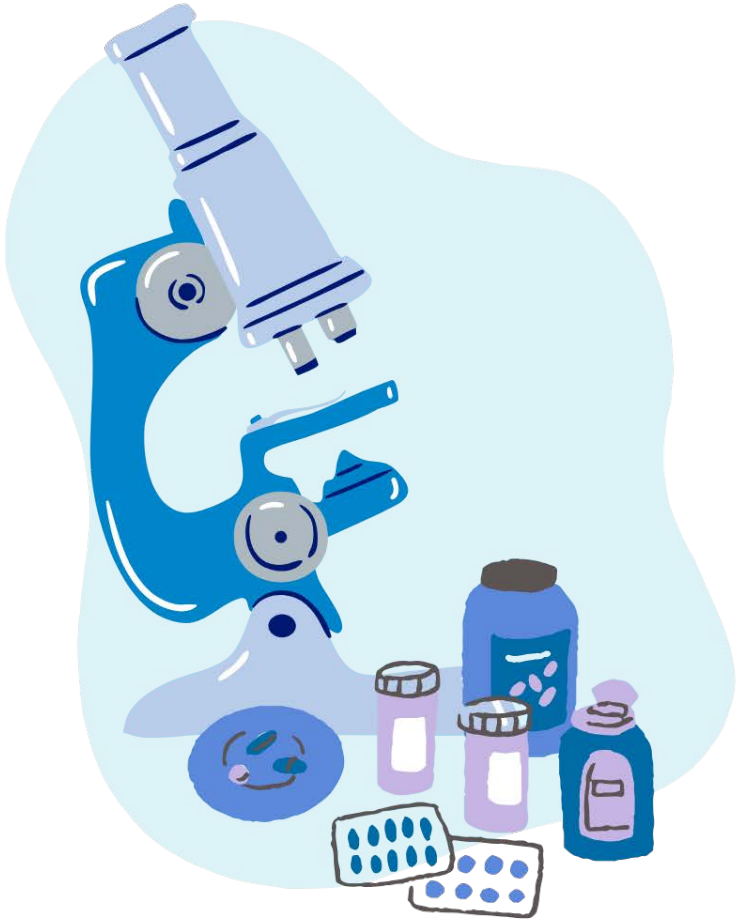
PQR principles

GMP agreement in place for responsibility for PQRs with APs

- Compilation
- Mechanism for access to AP
- Information with confirmation declaration

Information for the Authorised Person

On-going Stability principles



The manufacturer(s) performing release for supply and the sponsor share the responsibility to ensure an ongoing stability program of the finished product is conducted.

GMP agreement details mutual responsibility for:

- Mechanism for access to AP
- Information with confirmation declaration

Mechanism for AP access to ongoing stability data.

Information for the Authorised Person

Audit principles

- Know your supply chain
- GMP agreement details mutual responsibility-
  Mechanism for access to AP
  Information provided with confirmation declaration
  Can be provided directly to AP with certification

Information for the Authorised Person

Audits

- Procedure on audits
- What is an “audit” and “audit report”
- Audit report available if requested

Information for the Authorised Person

Other PQS items

Principles

- Ensure the following have been closed or assessed to not have a product impact
- Open deviations
- Complaints
- Change controls
- Validation

Information for the Authorised Person

Principles for certification

- Know the entire supply chain
- GMP agreement in place with all APs for key responsibilities.
- Access to all Confirmation declarations for PQS
- Perform the release for supply step

Confirmation declaration

Example

Batch certification declaration:

- name, text on finished product package
- Batch number and destination
- Name and address of site for partial manufacture
- Reference to the GMP agreement in place
- Confirmation that all manufacturing steps have been carried out in full compliance with GMP and as applicable with marketing authorisation or equivalent
- Name and signature of the Authorised person and date

Ensure declarations are accurate.

Confirmation declaration

Example

- Example declaration content:
  - No open deviations/OOS/complaints/change controls
  - No open audit findings
  - The validation and qualification status is current
  - No adverse PQR and ongoing stability information that will impact batch release
- Mechanism for the PQR and ongoing stability information to be provided to the AP as per GMP agreement
- “Audit reports” to be provided if requested as per GMP agreement.
- Certificate of analysis

Release for supply (batch certification)

Bringing it all together!

Batch certification declaration

- name, text on finished product package
- Batch number and destination
- Certification that all manufacturing steps have been carried out in full compliance with GMP and as applicable with marketing authorisation or equivalent
- Name and signature of the Authorised person and date

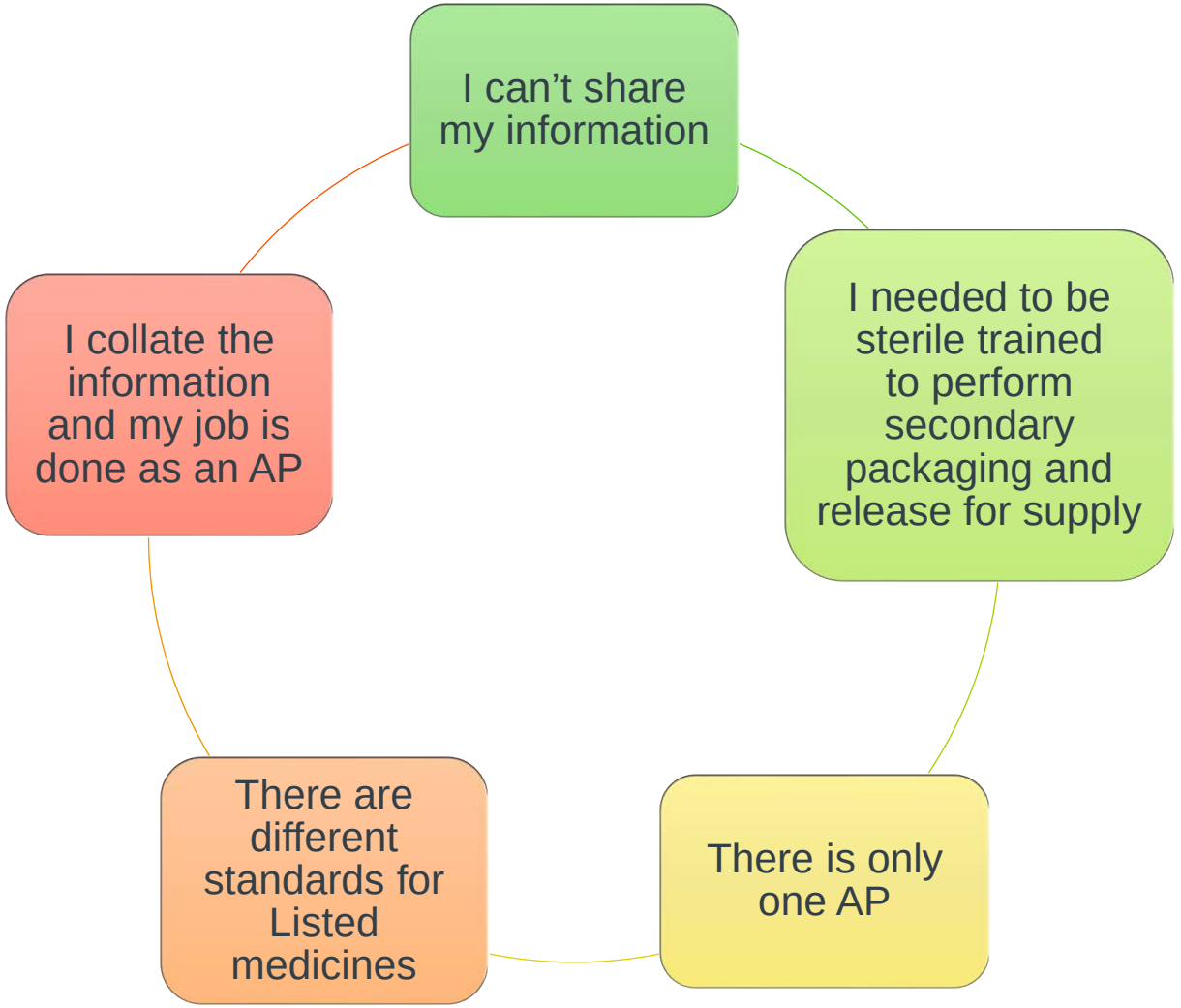
Ensure declarations are accurate.

Release for supply (batch certification)

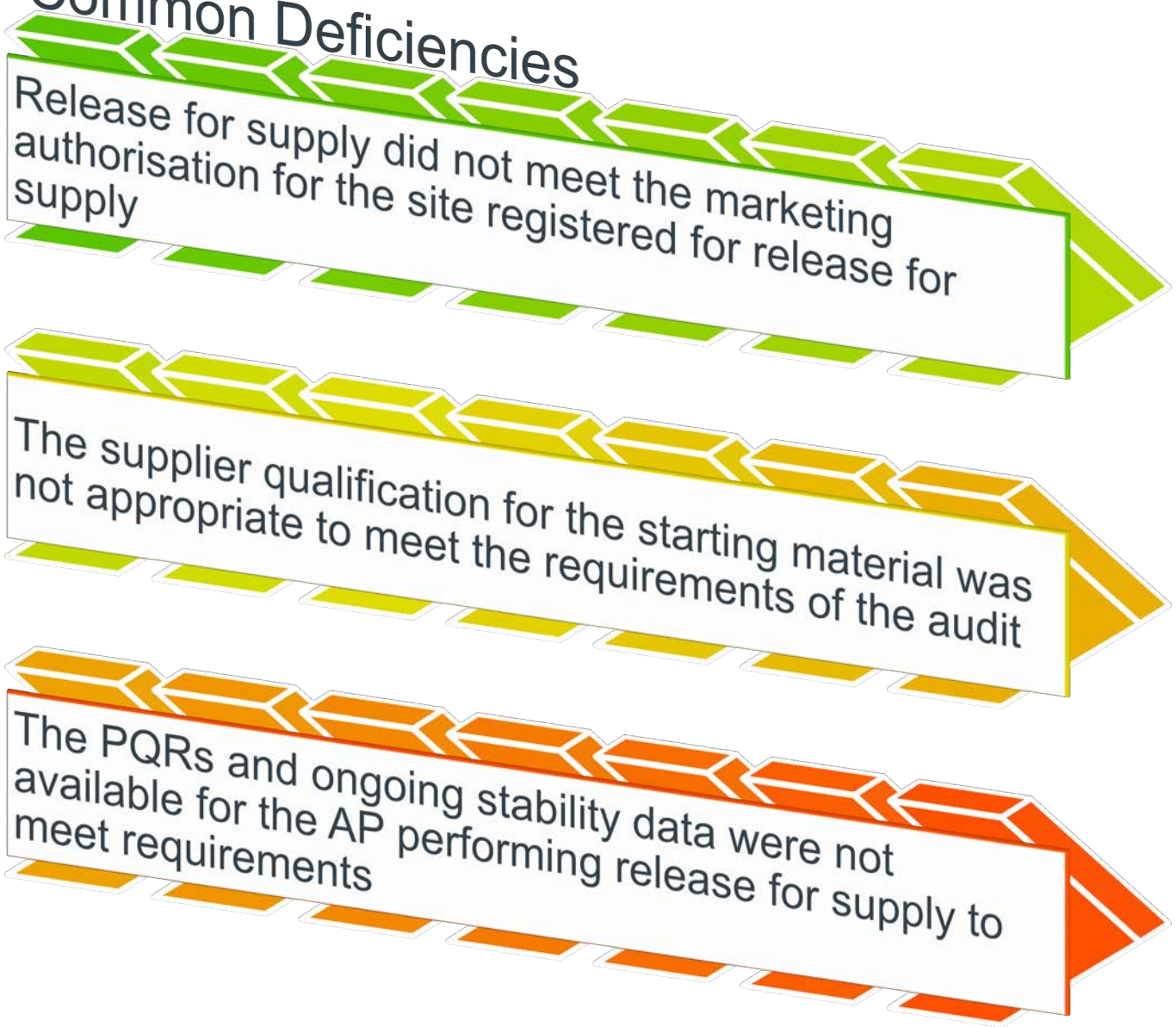
Bringing it all together!

- The following is a consideration for the declaration for completeness to confirm they have been checked
  - No open deviations/OOS/complaints/change controls
  - No open audit findings
  - The validation and qualification status is current
  - No adverse PQR and ongoing stability information that will impact batch release
- Mechanism for the PQR and ongoing stability information be provided to the AP as per GMP agreement
- “Audit reports” to be provided if requested as per GMP agreement.
- Certificate of analysis

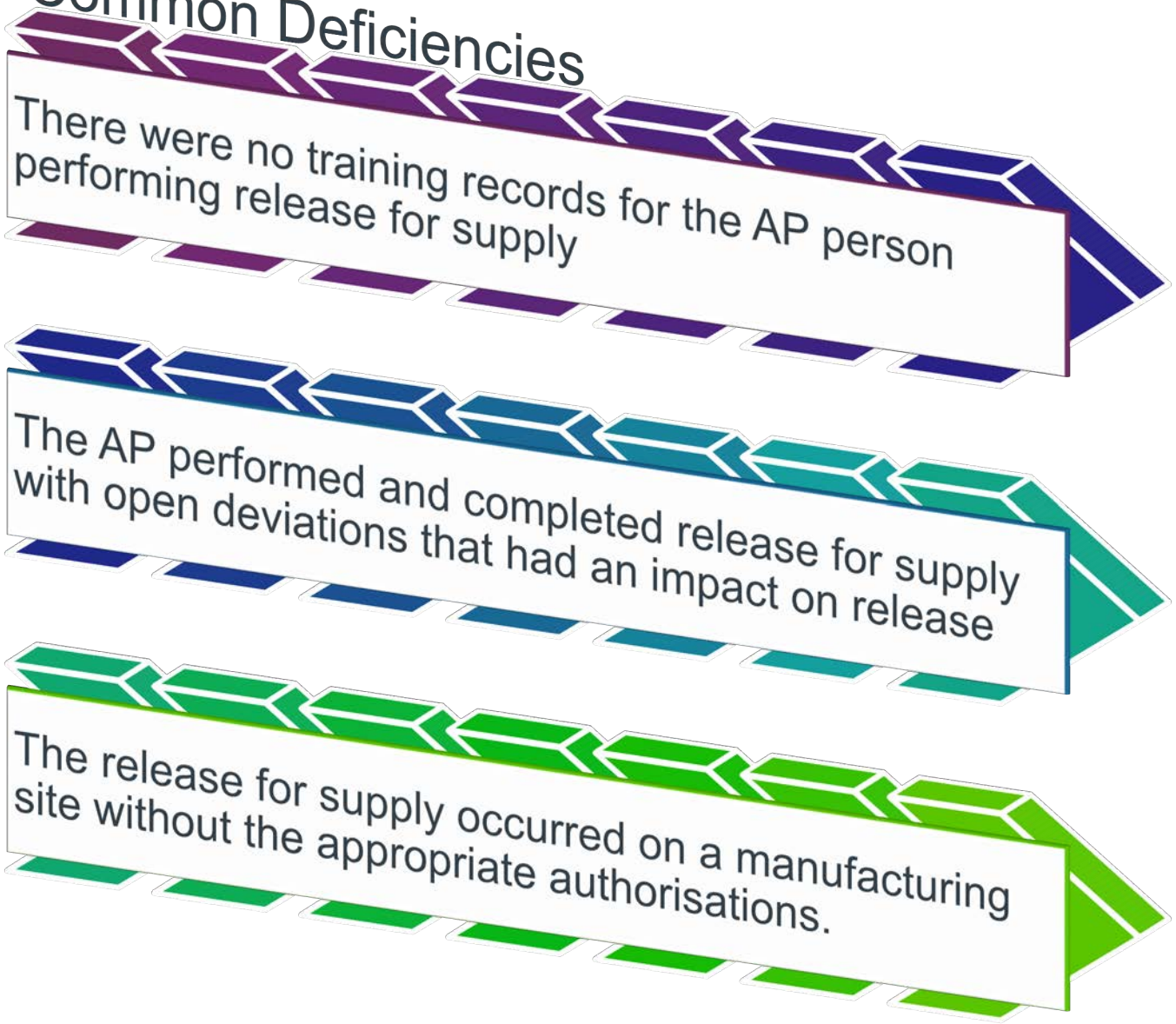
Myths going around about release for supply



Common Deficiencies



Common Deficiencies



Scenario

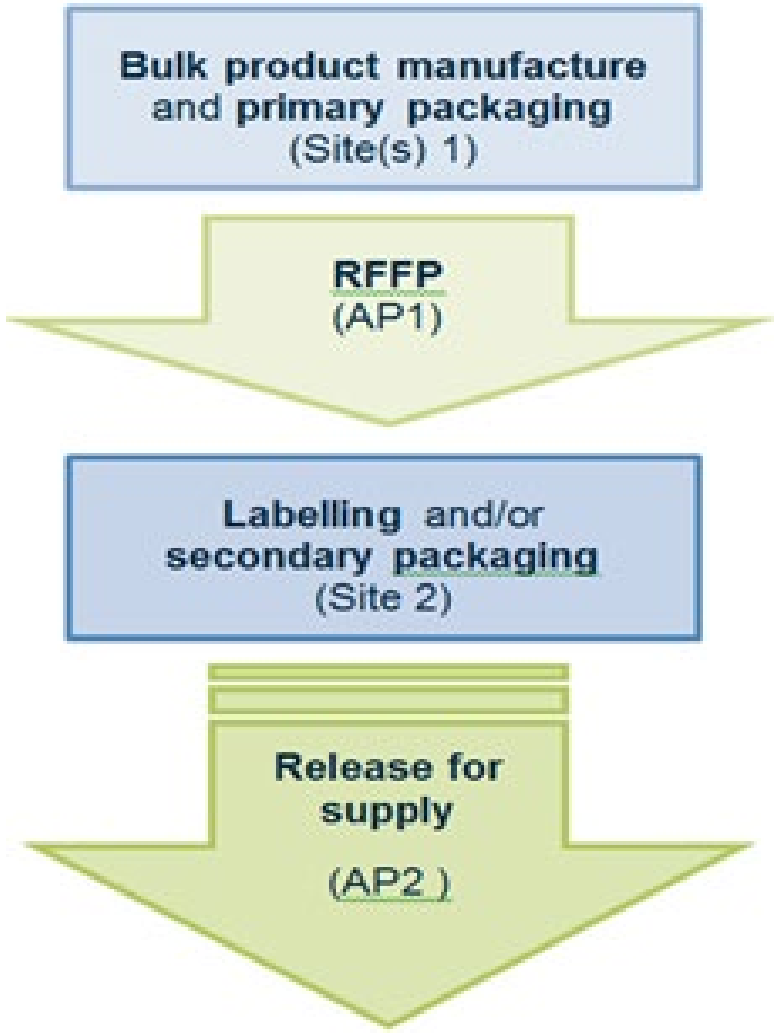
Let’s work through this example

Authorised person 1- Confirmation

- ✓ Confirmation Declaration
- ✓ Declaration package – full PQR, ongoing stability, audits, certificate of analysis

Authorised person 2- Certification

- ✓ Certification declaration
- ✓ Rely on Confirmation declaration package from site 1.



Summary

What we covered today

- What is Annex 16
- Authorised person requirement
- Purpose of batch release
- New terms
- Information for the Authorised Person and example declarations
- Release for supply (batch certification)
- Myths
- Common deficiencies
- Scenario

Questions?

Scan this QR code with your device to submit a question

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Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration