Submitting Effective GMP Clearance Applications

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GMP FORUM 2024

Agenda

- What are effective applications?
- How to submit an application
- Variation applications
- Evidence
- Questions

Introduction

Good Manufacturing Practice (GMP) Clearances are used:

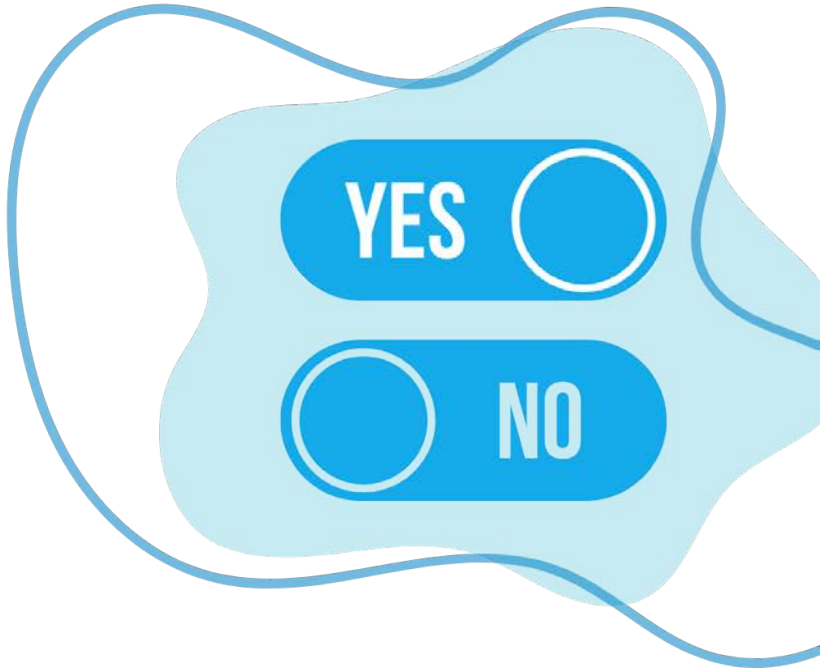
- For overseas manufacturing sites
- To verify compliance with principles of GMP
- Support registration or listing on the ARTG
- Sponsors are responsible for obtaining and maintaining clearances

Sponsors can apply for a GMP Clearance using one of the three pathways:

- Mutual Recognition Agreement (MRA) pathway
- Compliance Verification (CV) pathway
- An inspection by the TGA

What is an Effective Application?

- It is complete and contains all relevant information
- Appropriate fees have been paid (no additional invoices need to be raised)
- The correct scope has been selected
- All required evidence is submitted



Effective applications progress through the receipting and assessment process without having a stop clock applied (status ‘with manufacturer’)

Mutual Benefits of Submitting an Effective Application

Industry

- Avoid unnecessary delays
  - Invoices and payments
  - Evidence and RFIs

- Avoid updating your ARTG entries by maintaining the original GMP Clearance number
- Prevent validation issues with the regulatory submission system
- Get the maximum clearance validity (where possible)
- Save money

TGA

- Reduction of manual invoicing
- Reduce risk of impact to registrations
- Reallocate resources for process improvements
- Reduce number of ‘not issued’ clearances
- Reduces the number of RFIs which need to be sent

How to Submit an Application

Which application to submit?

New Application
First time applying for a manufacturing site

Variation application (already hold an active clearance)
Renew the clearance
Make a change • Increase or decrease the scope • Update the manufacturer details • Update the sponsor or agent's details
Request an extension
Request a cancellation

Submitting a New GMP Clearance Application

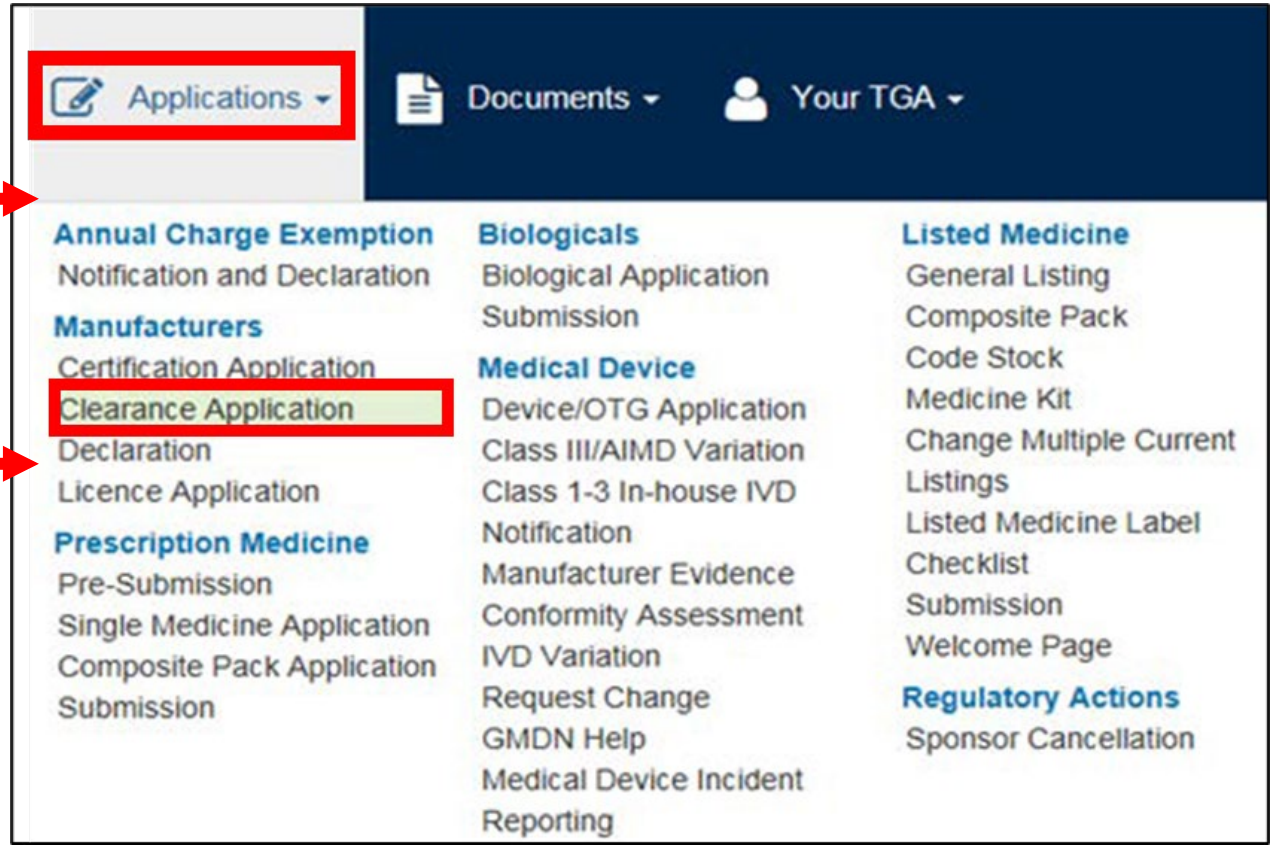
To create a new application:

Login into the TGA Business Services portal

1. Click Applications

then

2. Select Clearance Application

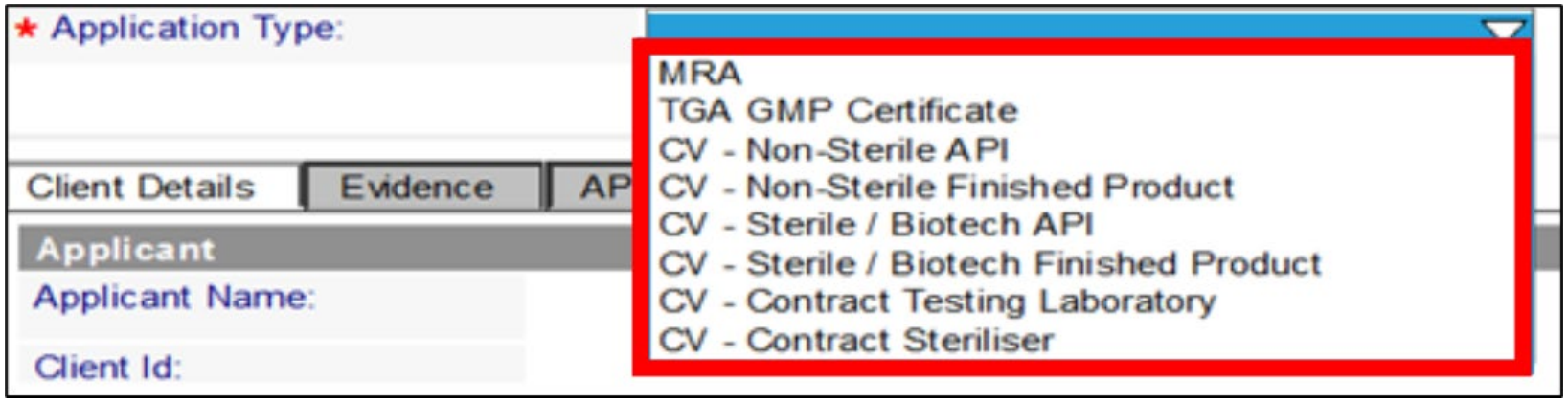


Selecting the Application Type

New GMP Clearance applications:

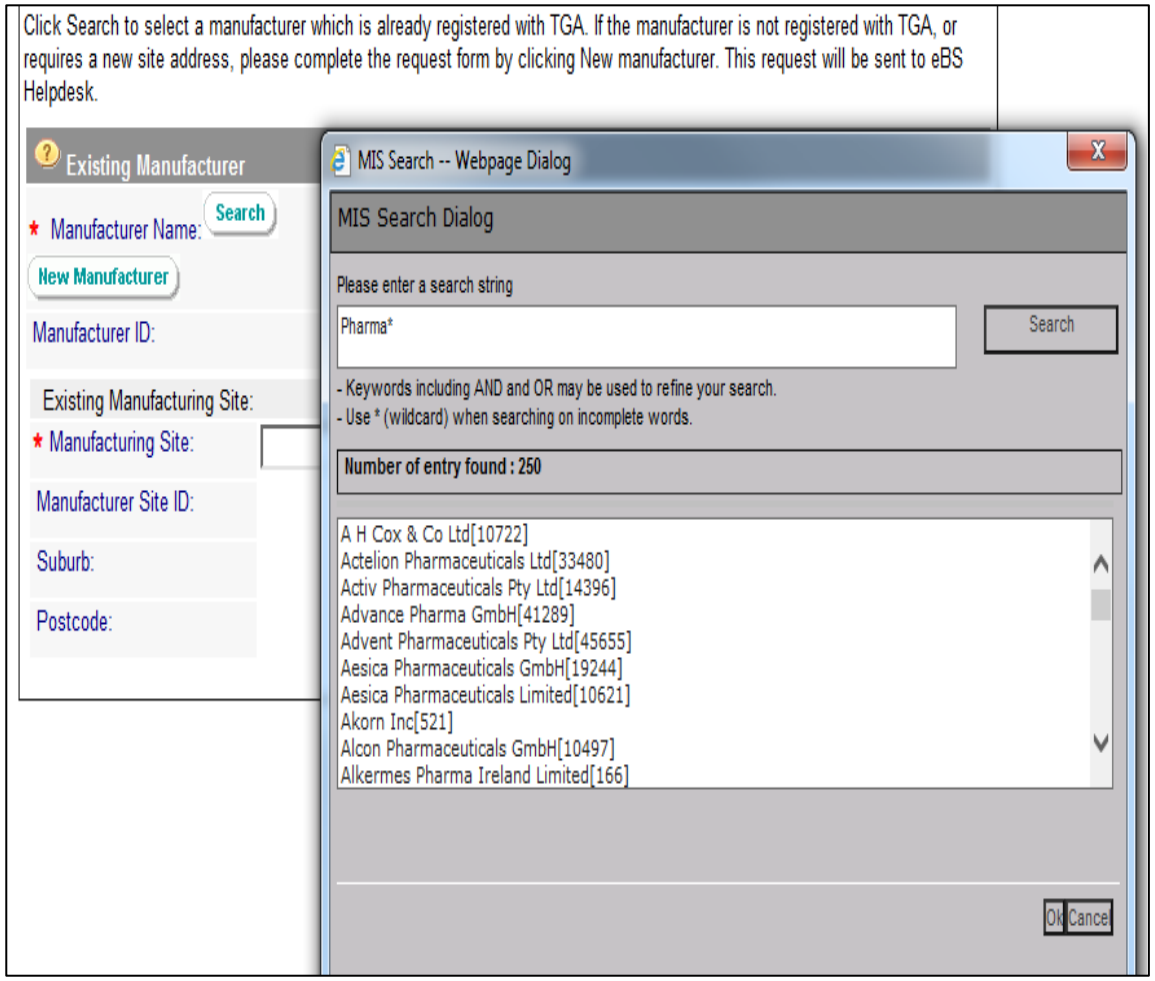
- The application type determines what evidence is required
- The application type cannot be changed after submission

ℹ If you select the incorrect application type:
  - Your application may be delayed
  - You may need to submit a new application



Selecting the Manufacturer Name

New GMP Clearance applications:



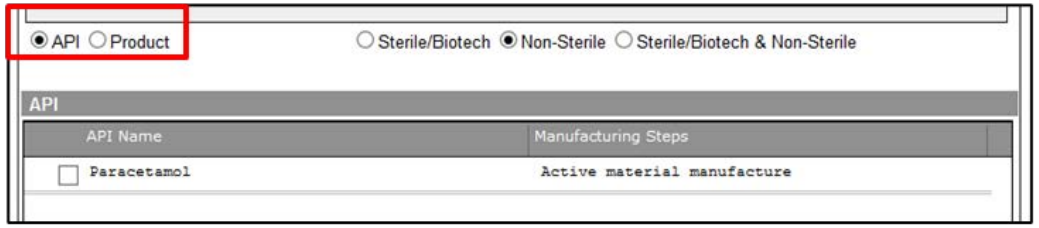
- Check the manufacturers in the system before requesting a new manufacturer
- Where the site's name has changed:
  - Select the company's old details
  - Submit evidence and request an update as part of the new application
- Contact us before requesting a new manufacturer entry

Duplicated manufacturing sites can extend processing times and may require significant updates to your ARTG entries.

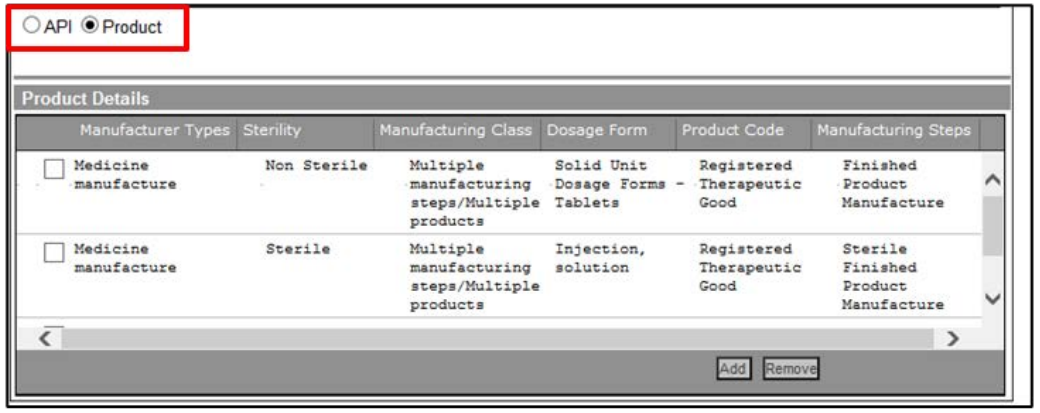
Selecting the Application Scope

New GMP Clearance applications

API scope



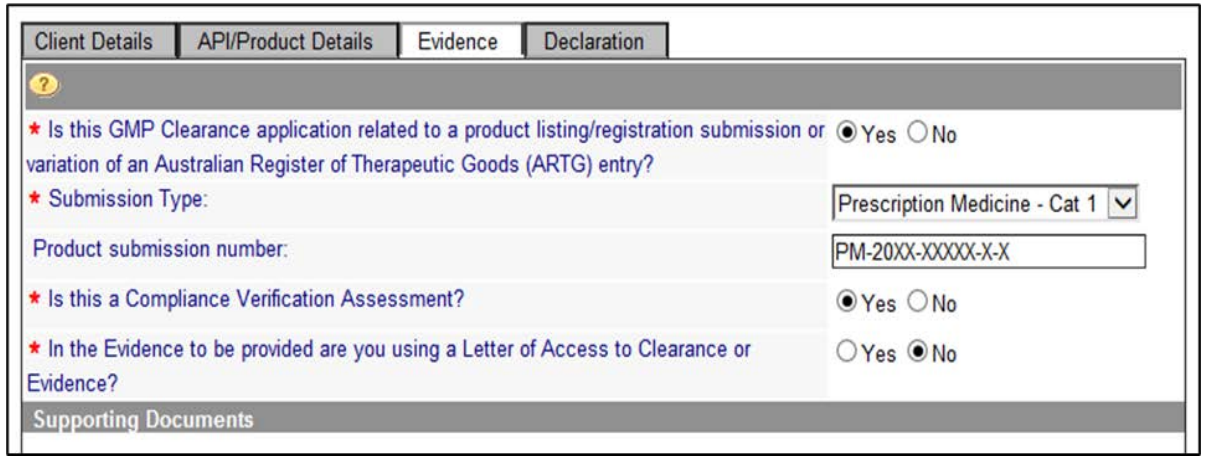
Product (dosage form)



- Your application scope determines what evidence is required
  - o API / Product
  - o Sterility
  - o Dosage form
  - o Manufacturing steps
- **Separate applications** need to be submitted for API and finished product scopes
- You should ensure your evidence supports your scope

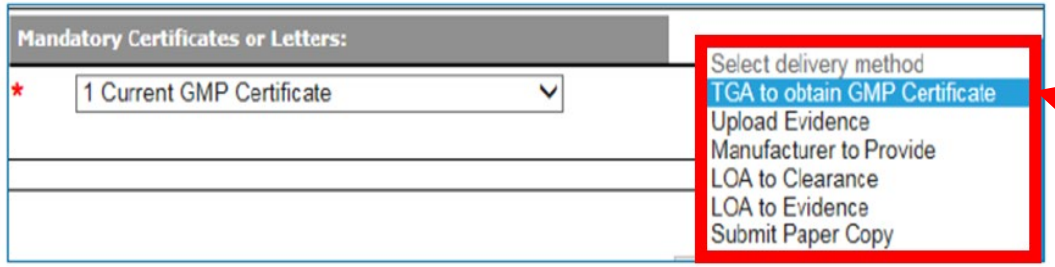
The application cannot be amended to the correct scope later if the wrong one is selected during submission.

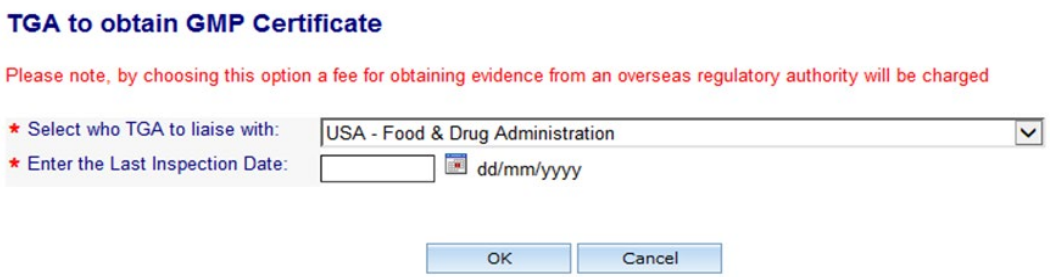
Registration/Listing and ARTG Updates

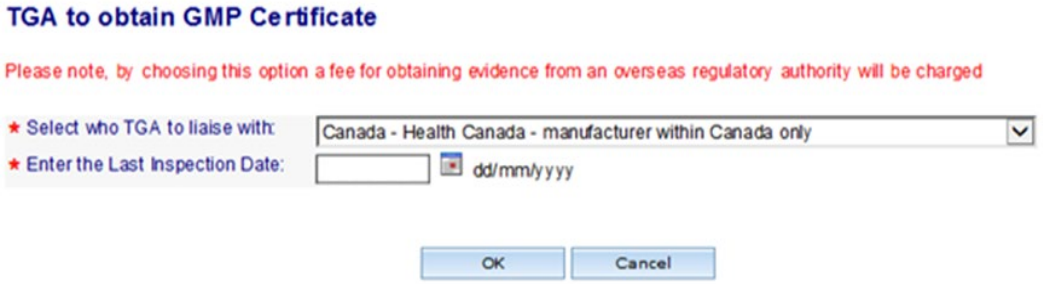


- For applications related to registration / listing, include:
  - Milestone date details
  - Product submission number
- Provide a cover letter for additional details or clarification as necessary
- This information assists us to effectively process and prioritise applications

Payment of Fees







US FDA and Health Canada (HC)

- For **CV applications** using US FDA or HC evidence, select TGA to obtain GMP Certificate
- **<u>Do not</u>** upload a document for the 'current GMP Certificate' as this will cause a delay
- Upload the US FDA inspection report or HC Exit Notice under the most recent inspection report

If you do not select 'YES' to this question and it is a CV application, the application will be delayed until the fee is paid.

Submitting a Variation Application

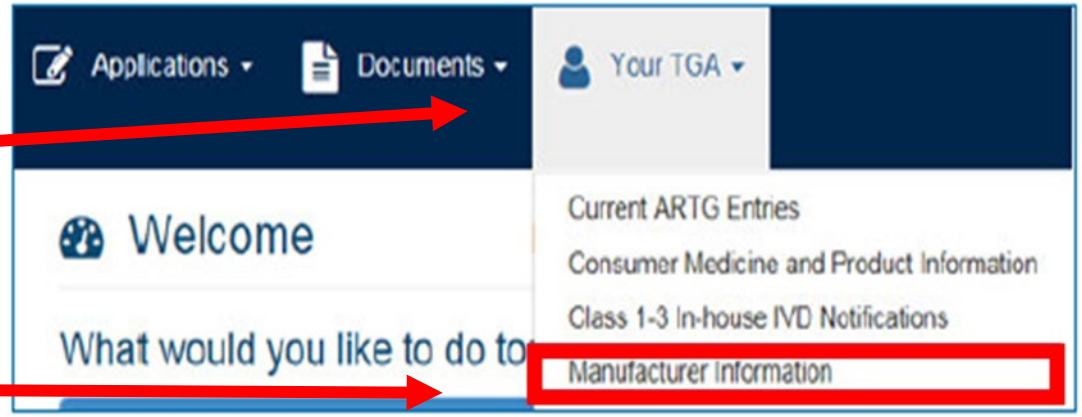
- To create a variation application:

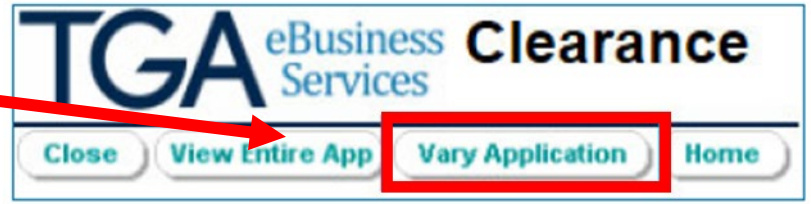
- Log into TGA Business Services portal,
  1. Click **Your TGA**

  2. Select **Manufacturer Information**

  3. Filter clearances using 'CL' and select relevant clearance

  4. Select **Vary application** from the menu bar at the top of your GMP clearance





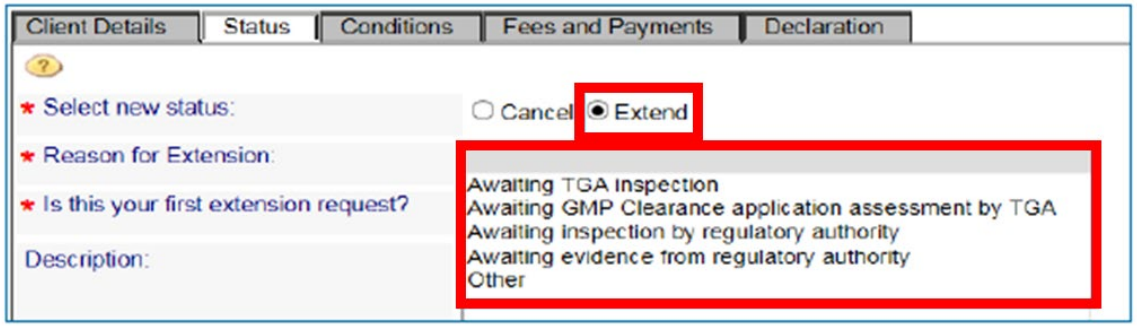
Maintenance of Active GMP Clearances

Status:	Active
Tracking Number:	MI-2022-CL-01234-1
Original Tracking Number:	MI-2019-CL-04567-1
Application Type:	CV - Non-Sterile Finished Product

Variation Applications

- Submit a variation application if you already hold a clearance
  - This maintains the link to your existing clearance
- Variation applications will receive a temporary, in-process number when submitted:
  - This reverts to the original tracking number (e.g. MI-2019-CL-04567-1) once the application is approved
  - This avoids the need to update ARTG entries
- Variation applications can only be submitted up to 30 days past expiry

Extensions



Variation Applications

- Extensions can be issued for valid reasons
  - Check for new GMP evidence prior to submission
  - Submit a renewal application if new evidence is available
- In ‘Description’ include the explanation for the request
- Evidence may be required to support extension requests
- A TGA inspection may be required if you cannot provide updated supporting evidence

Evidence

CV pathway	Non-Sterile API	Non-Sterile Finished Product	Sterile or Biotech API	Sterile or Biotech Finished Product	Contract Testing Lab or Steriliser
GMP Certificate	✓	✓	✓	✓	✓
Most recent inspection report	✓	✓	✓	✓	✓
Regulatory inspections list	✓	✓	✓	✓	✓
Regulatory action details	✓	✓	✓	✓	✓
Site Master File (SMF), quality manual or equivalent	✓	✓	✓	✓	✓
List of products intended for supply	✓	✓	✓	✓	✗
GMP agreement or equivalent	ⓘ	✓	ⓘ	✓	✓
Release procedure(s)	ⓘ	✓	ⓘ	✓	✗
Validation Master Plan (VMP)	ⓘ	ⓘ	✓	✓	ⓘ
Latest Product Quality Review (PQR)	ⓘ	ⓘ	✓	✓	✗
List of authorised tests	✗	✗	✗	✗	✓

✓ = Required ✗ = Not Required ⓘ = Not required unless requested

Application Requirements

- Provide all supporting documentation as per the GMP Clearance Guidance
- You need to provide all relevant evidence when submitting both new and variation applications
- Provide an API declaration where required for both MRA and CV applications
- Your application will be delayed or not issued if all required evidence is not provided

Evidence

Cover Letters

Cover letters should be used to provide additional clarification and information:

- Specific details of activities performed at the site
- Changes to the manufacturer details (name or address)
- Absence of evidence (where appropriate)
- Regulatory submissions (submission details, related applications)
- Medicine shortages or prioritisation

Evidence

Letter of Access (LoA)

LoAs can be used to access:

- An issued GMP Clearance
- Evidence which has been previously submitted

The type of LoA should be defined in the Letter of Access from the other sponsor or manufacturer:

- LoA to evidence
- LoA to clearance

Ensure the evidence or the clearance scope is identical or greater than the application being submitted

For LoAs to Clearance: The reference clearance must fully cover the scope of your application. Where this is not the case the scope will be amended or the clearance will not be issued.

An LoA cannot reference a clearance which was issued using another LoA.

Evidence

TGA Certificates

A TGA inspection may be required when:

- There is no supporting evidence available
- There are compliance issues

For contributing sponsors to a TGA inspection

- You do not need to submit another GMP Clearance application
- The TGA certificate will be issued to the manufacturer
- You will then be issued with a corresponding GMP Clearance

If you decline to contribute to a TGA overseas inspection without reasonable justification, we will not issue a GMP Clearance to you.

Evidence

GMP Clearance Questionnaire

Introduced as a requirement during the COVID-19 pandemic:

- Provides additional information for assessment
- Used where the inspection report is >3 years old

Ensure	The form is filled out completely
Ensure	Both parts of the form are provided
Provide	A separate document with further details if not enough space is available

Questions?

Scan this QR code with your device to submit a question

GMP FORUM 2024

Australian Government

Department of Health and Aged Care

Therapeutic Goods Administration