Australian Government
Department of Health
Therapeutic Goods Administration

# How to Submit an Effective Good Manufacturing Practice (GMP) Clearance Application

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TGA Health Safety Regulation

# Welcome | How to Submit an Effective Good Manufacturing Practice (GMP) Clearance Application

- This webinar is being recorded
- Slides will be made available on the TGA website
- To ask a question, use the message feature on the left of the screen
  - Messages will only be visible to the moderator and speaker
  - Questions will be answered at the end of the presentation
- Relevant links will be posted in the message box (below)
- Live polls will be conducted throughout this event.


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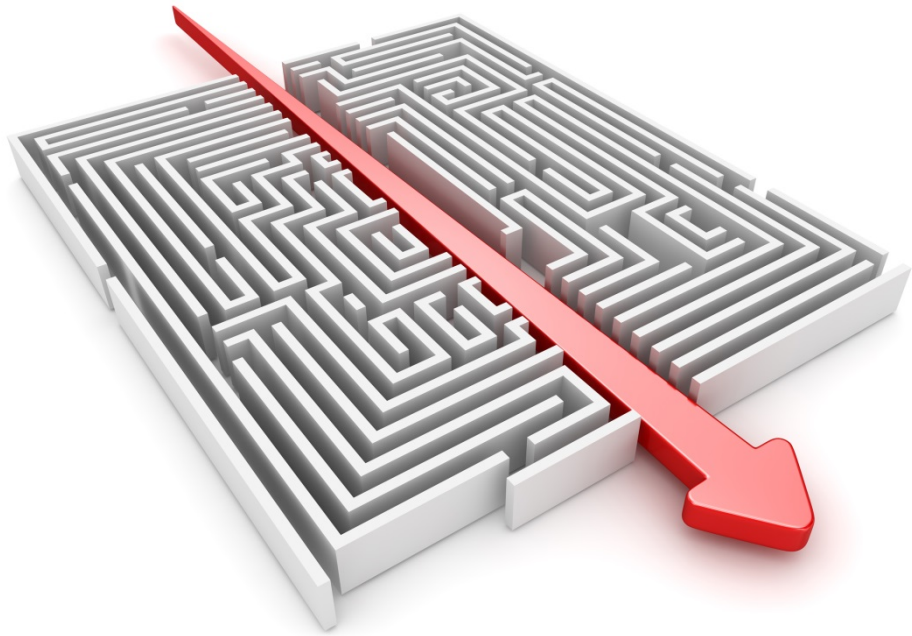
2. Enter Pass Code 1330247191
3. If difficulties still continue please contact Redback services for support on 1800 733 416

# GMP clearances - Background

- Good Manufacturing Practice (GMP) Clearances are used to verify that overseas manufacturing sites comply with the principles of GMP for products being supplied to the Australian market.
- Sponsors are required to obtain GMP clearances for overseas manufacturers to register or list their products on the Australian Register of Therapeutic Goods (ARTG).
  - It is the sponsor's responsibility to maintain the currency and accuracy of the GMP clearance.
- Two desk top GMP clearance pathways are available
  - Mutual Recognition Agreement (MRA) pathway
  - Compliance Verification (CV) pathway

# What is an effective application?

- The application is complete and contains all relevant information
- Appropriate fees have been paid (no additional invoices need to be raised)
- The correct application 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 with your application
  - Payments can be processed effectively
  - Receipting process more efficient
- May reduce processing times
- Maintain the original GMP clearance number
- Avoid the need to update your ARTG entries
- Prevent validation issues with the regulatory submission system
- Get the maximum clearance validity (where possible)
- Clearance scope not reduced
- Save money

**TGA**

- Reduction of manual invoicing
- Reduce risk of impact to registrations
- Reallocate resources for process improvements
- Reduce number of ‘not issued’ clearances

# Submitting a GMP clearance application

- **New** or **variation** applications may be submitted
- By submitting variation applications for manufacturing sites, where an active clearance is already held, the original clearance number is retained.

| New Application | Variation application (when an active clearance is held) |
|---|---|
| First time applying for a clearance for a manufacturing site | Renew the clearance |
| | Make a change<br>• Vary the scope (increase or decrease)<br>• Update the manufacturer details (name and address changes)<br>• Vary sponsor or agents details |
| | Request an extension |
| | Request cancellation |

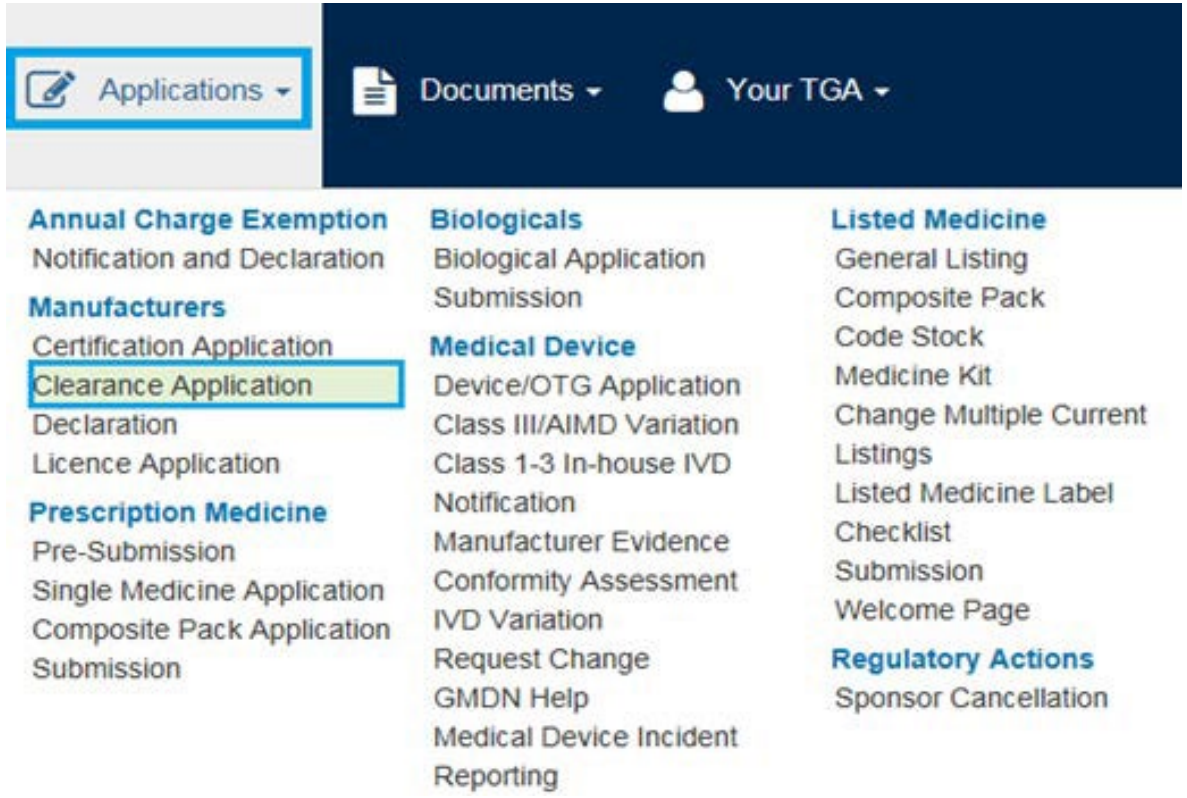
# Submitting a New GMP Clearance Application

To create a new application:

- Login into the TGA Business Services portal
  a) Click **Applications**

  then

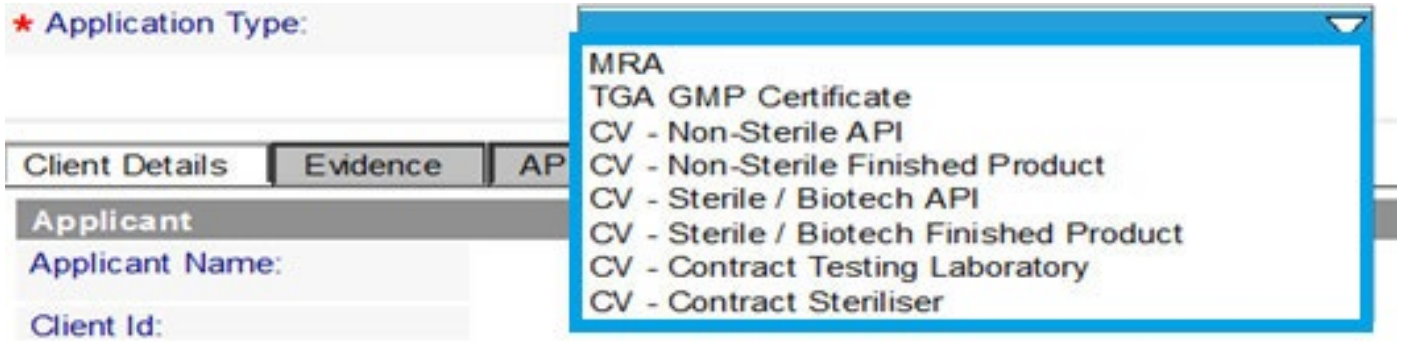
  b) select **Clearance Application**



# Selecting the application type

## New clearance applications

- The application type determines what information is required for your application.




After an application is submitted the application type cannot be changed.

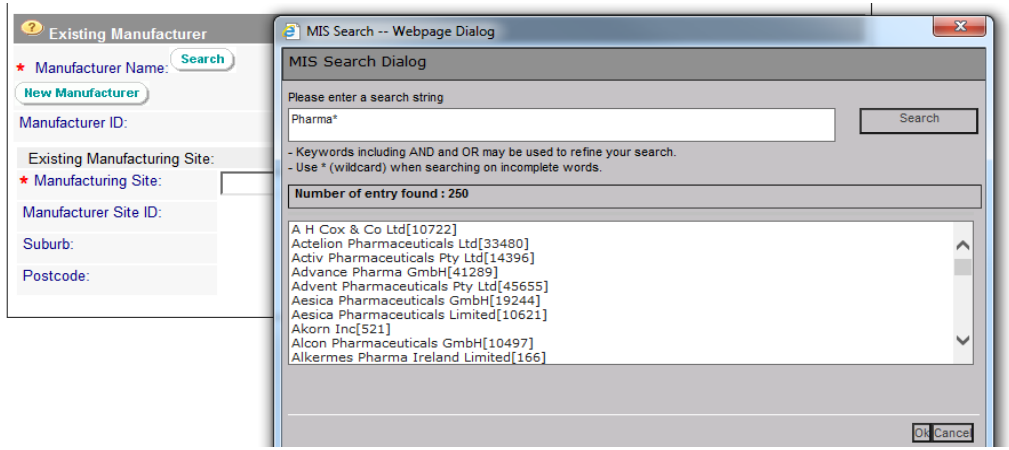
If the incorrect application type is selected:

- Your application may be delayed
- You may need to submit a new application and pay the applicable fees.

# Selecting the manufacturer name

## New GMP clearance applications

- Thoroughly check the manufacturers in the system prior to requesting a new manufacturer.
  - Check the name and address
  - Consider if any recent changes to the company name and address have occurred as this may impact the entries in the system.
    - If a company's name or address details have changed and only the old manufacturer details display in the system, you can select the existing entry, submit evidence and request an update as part of the new application.
    - New manufacturer entries can be created however please contact us before making this request.




When duplicate manufacturing site entries are created this can extend processing times and may require significant updates to your ARTG entries.

# Selecting the application scope

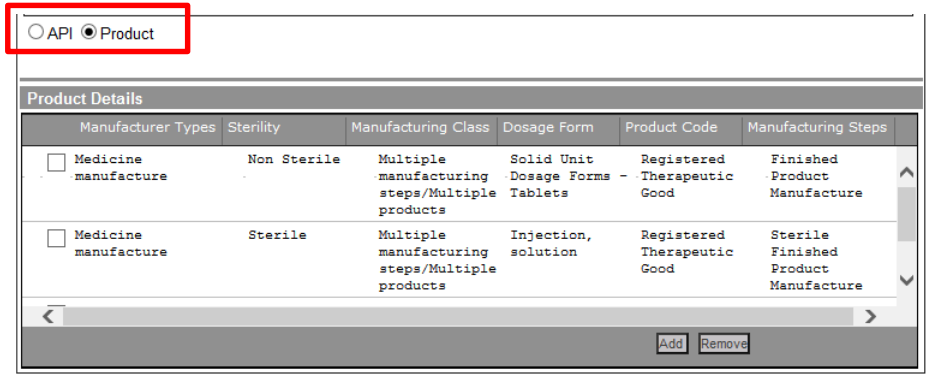
## New clearance applications

- Selecting the scope of the application determines what information is required.
- Options are:
  - API (Active Pharmaceutical Ingredients)
  - Product (dosage form)
- **Separate applications** need to be submitted for API and finished product scopes.

If an application is submitted with the incorrect scope in relation to API versus Product, the application cannot be amended to the other.

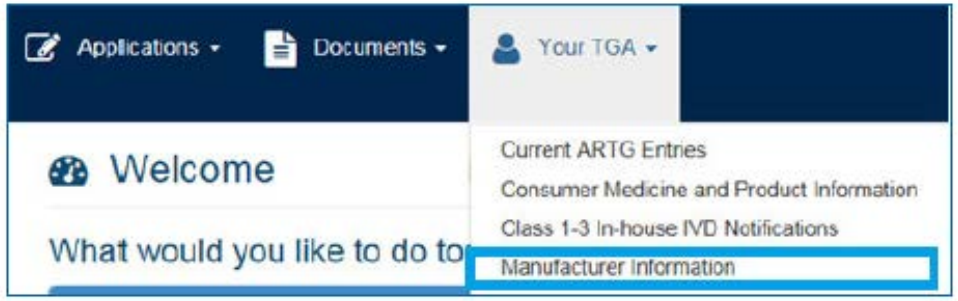
## API scope

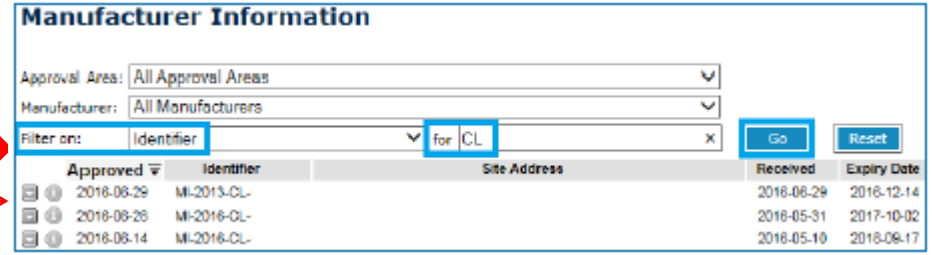

## Product (dosage form)



# Submitting a variation application

- To create a variation application:
- Log into TGA Business Services portal,
  a) Click **Your TGA**,
  b) select **Manufacturer Information**
  c) Filter clearances using ‘CL’ and select relevant clearance
  d) select **Vary application** from the menu bar at the top of your GMP clearance




# Maintenance of active GMP clearances

## Variation Applications

- If you hold an active clearance, submit a variation application rather than a new application.
- By submitting variation applications a temporary number is issued (this is an ‘in process’ number) for the application:
  - Revert to the original tracking number MI-20xx-CL-xxxxx-1
  - Avoid the need to update ARTG entries
- You can only submit variation applications for clearances up to 30 days past expiry, after this you will not be able to vary via the TGA Business Service Portal.

| | |
|---|---|
| Status: | Active |
| Tracking Number: | MI-2022-CL-01234-1 |
| Original Tracking Number: | MI-2019-CL-99999-1 |
| Application Type: | CV - Non-Sterile Finished Product |

# Tracking numbers

- When an application is submitted it will only have one tracking number

  E.g. MI-2017-CL-XXXXX-1

- When a renewal application is submitted, it will have two numbers, the original tracking number and the temporary tracking number associated with the application

  E.g. MI-2017-CL-XXXXX-1 (original tracking number)

  MI-2019-CL-YYYYY-1 (temporary tracking number for variation application)

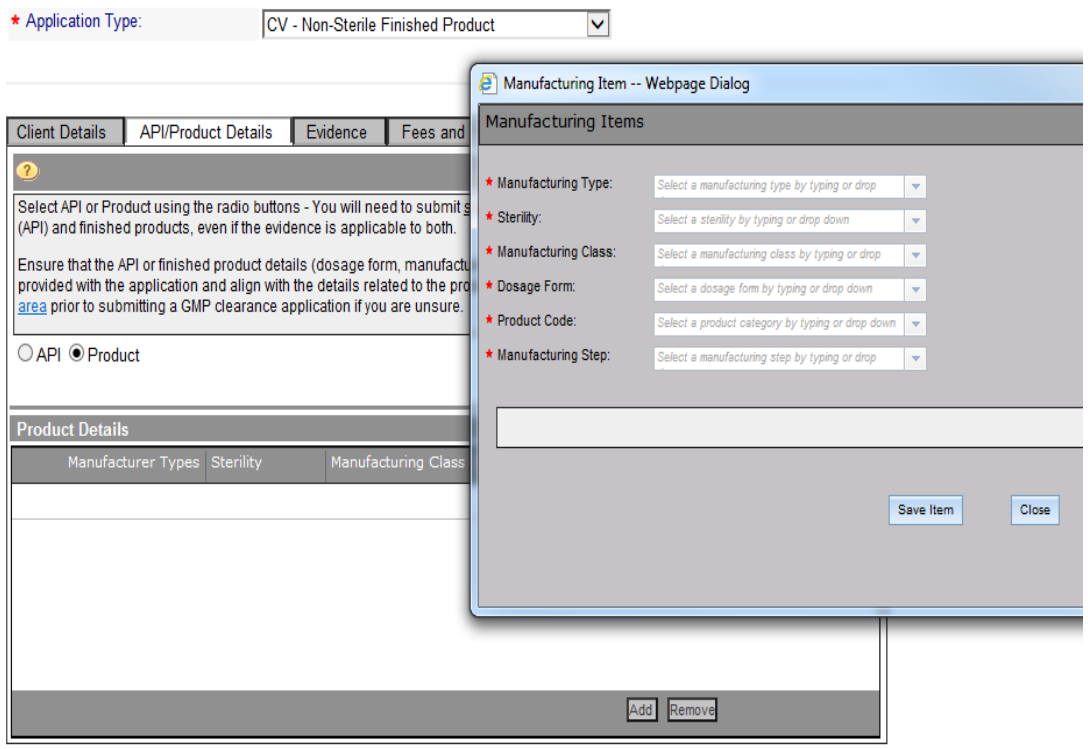
- After the application has been approved, the temporary tracking number will disappear from your view and you will only be able to see the original tracking number associated with the clearance and ARTG entry for the manufacturing site

  E.g. MI-2017-CL-XXXXX-1

# Application scope

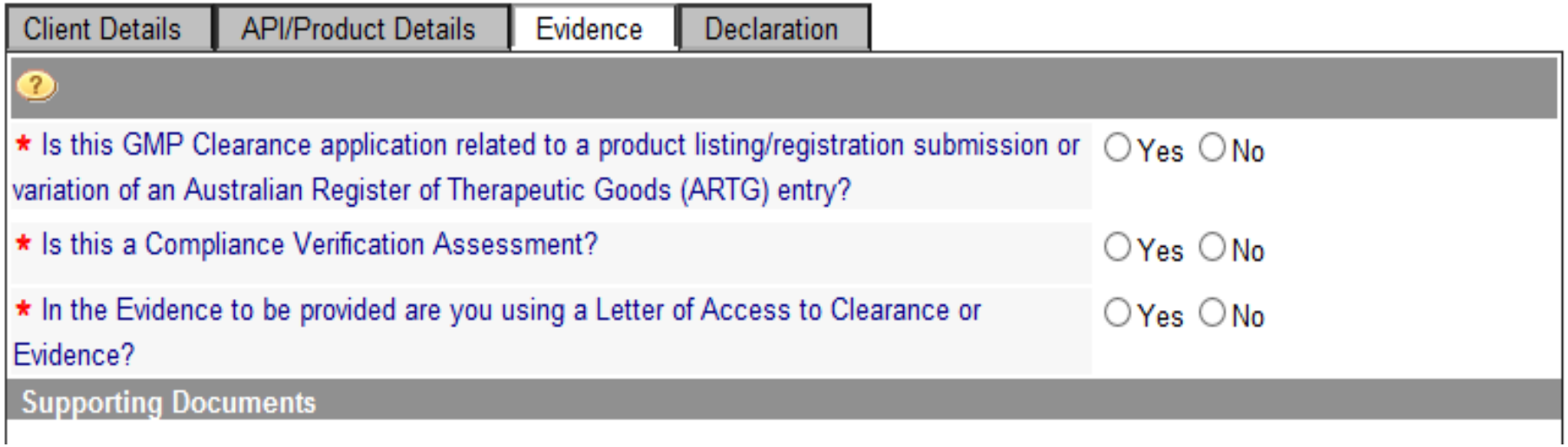
- The sponsor is responsible for determining the scope of the GMP clearance.
- Ensure the application scope – dosage forms and steps of manufacture are covered by the supporting evidence to be submitted with the application.
- Consider the validation rules of the relevant regulatory submission system when selecting the scope.
- If you have questions about whether you require a GMP clearance or if it aligns with the registration or listing requirements you should contact the relevant regulatory area of TGA prior to submitting an application.

Incorrect scope selections may lead to issues with product registration and listing activities.



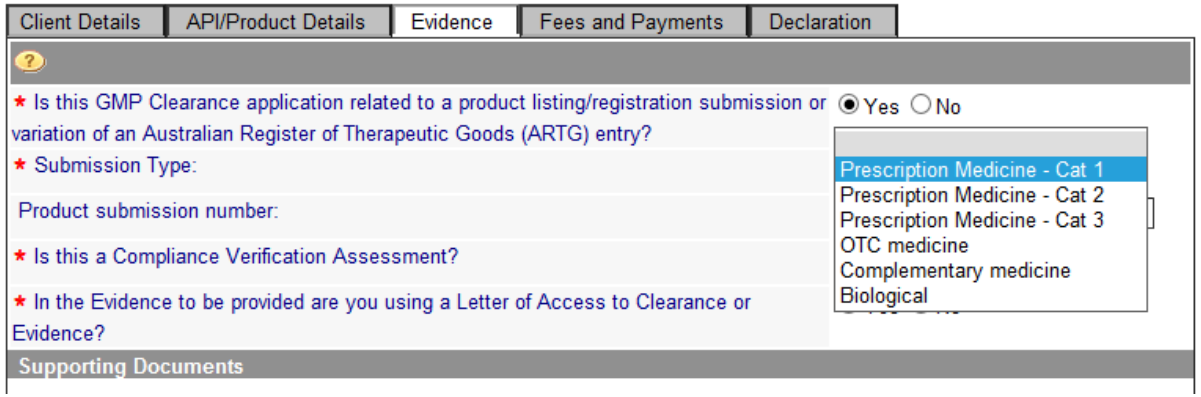
# Evidence and payment of fees

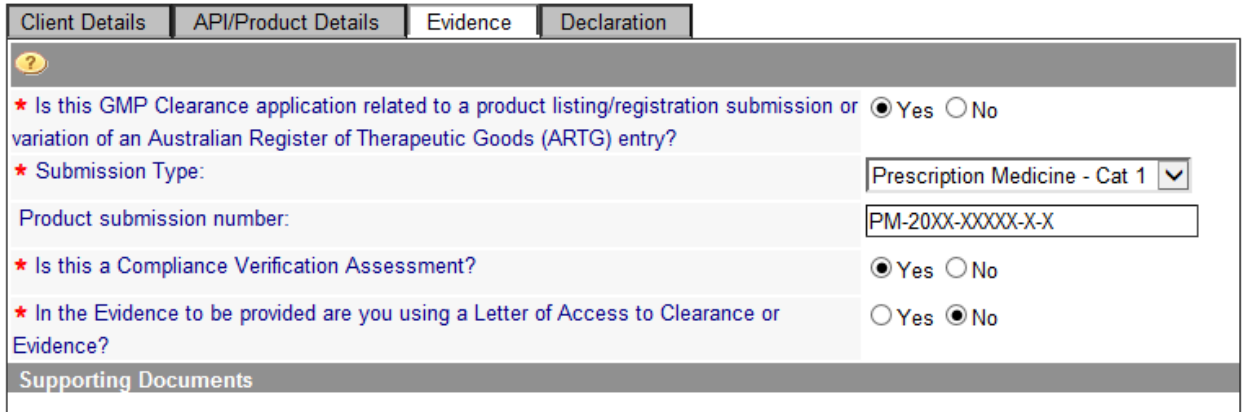
- There are a number of mandatory questions in the evidence tab which determine the type of evidence required. It is also where fees are determined.



# Registration/Listing and ARTG Updates

- If the application relates to a registration/listing or an ARTG update (variation to an existing entry), please provide the relevant information including:
  - Milestone date details (for new submissions)
  - Product submission number (if known)
    - If there is insufficient space to include the response please submit a cover letter with the submission details
- This information assists to effectively process applications

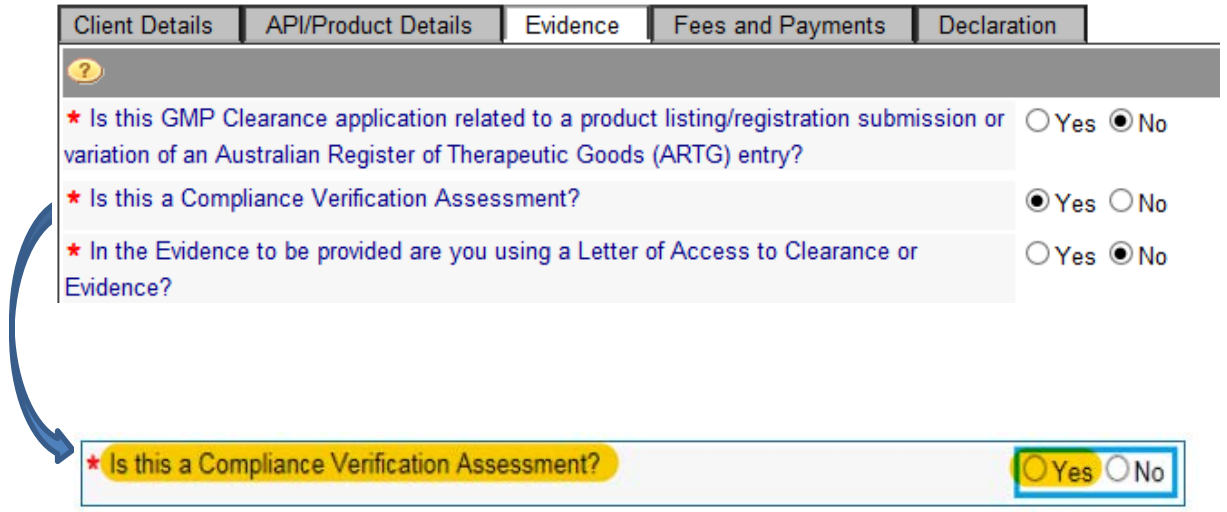


# Is this a Compliance Verification (CV) application?

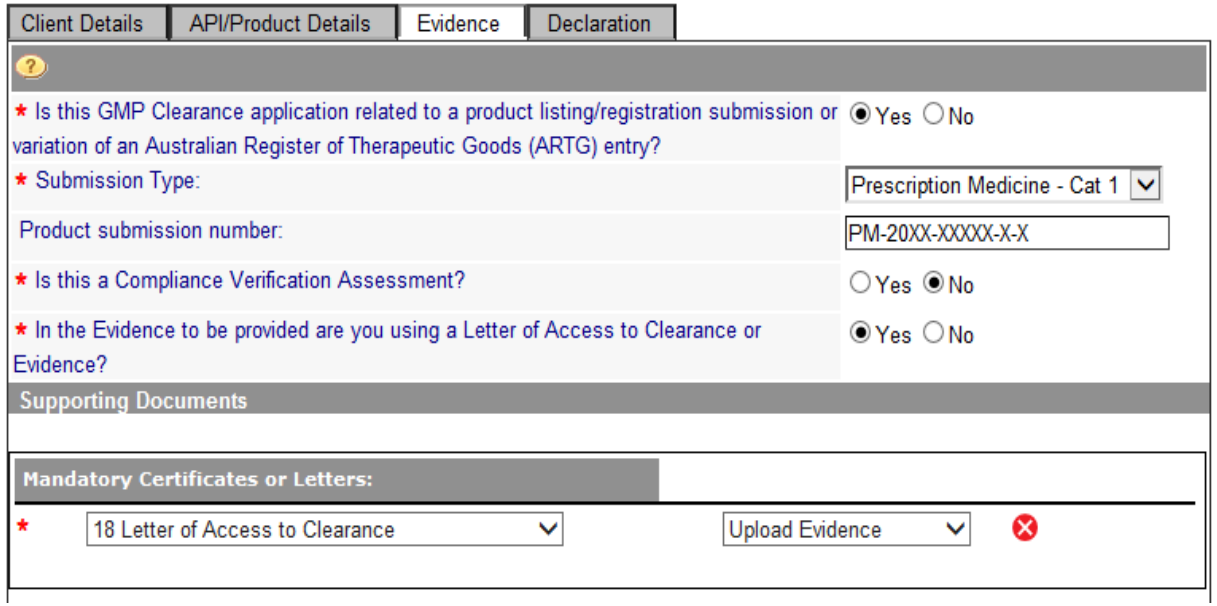
- If the application is a CV application, you must select ‘yes’ to the question *is this a compliance verification assessment* so the appropriate fee is raised.

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.



# Evidence: Letter of Access (LoA)

- If you intend to use a Letter of Access (LoA) to a clearance or evidence, please ensure the evidence or the clearance scope is identical or greater than the application being submitted.
- The type of LoA should be defined in the Letter of Access from the other sponsor or manufacturer:
  - LoA to evidence (either a manufacturer or sponsor grants another sponsor permission to access evidence they have previously submitted for another GMP clearance application)
  - LoA to clearance (a sponsor grants another sponsor permission to use their GMP clearance as primary evidence where the scope of the application is identical or smaller)

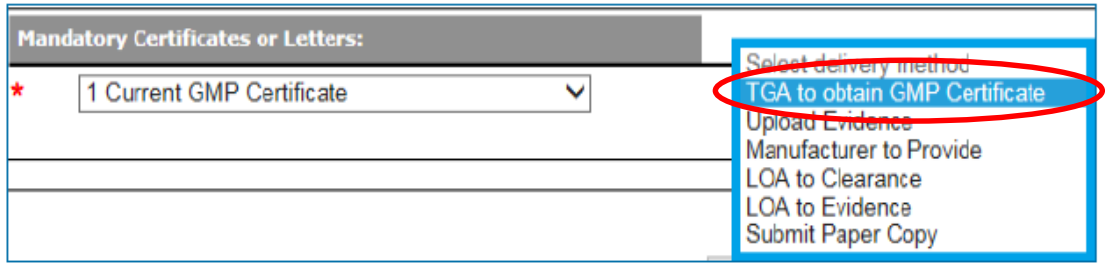



If the scope of the reference evidence or clearance does not cover the scope of the application, the application scope will be amended or a clearance will not be issued.

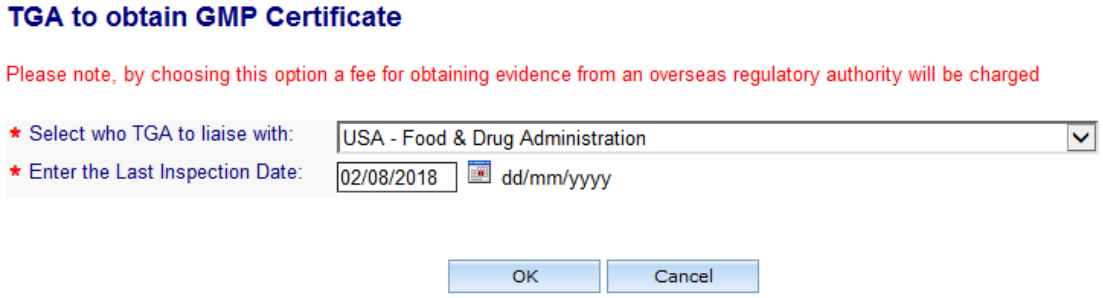
A LoA can only reference a clearance that has been issued based on full assessment of evidence and not from a clearance issued using a LoA.

# CV applications with US FDA evidence

- For sponsors using US FDA evidence to support CV applications **you must** select TGA to obtain GMP certificate.

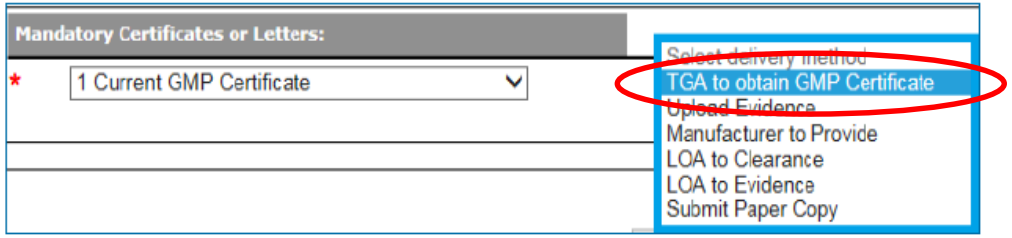



**Do not** upload the front page of the Establishment Inspection Report (EIR) as this will cause delay.



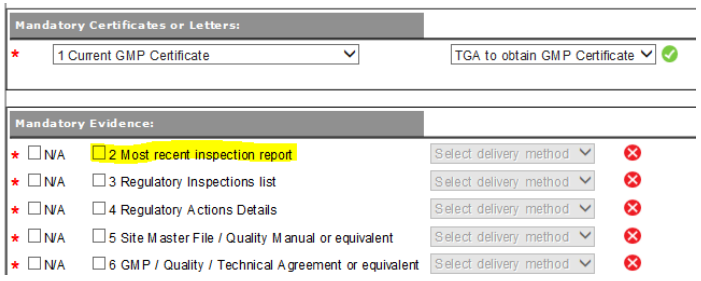
# CV applications with Health Canada evidence

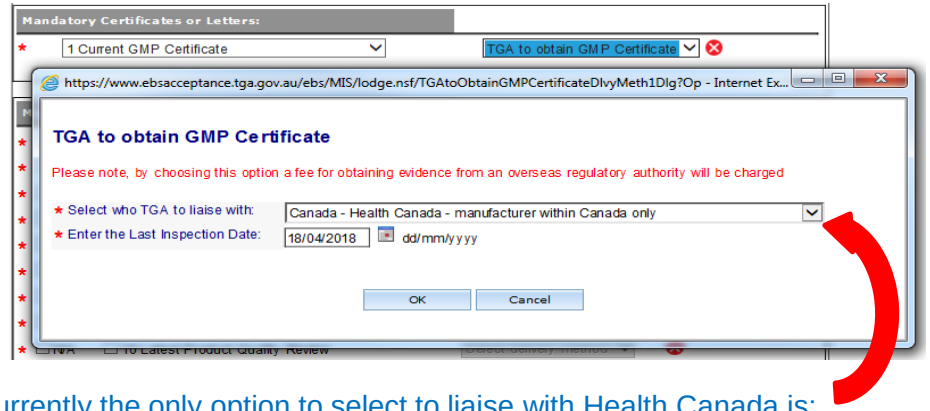
- For sponsors using Health Canada (HC) evidence to support CV applications **you must** select TGA to obtain GMP certificate.




For **CV applications, do not** upload the Exit notice as the current GMP certificate as this will cause delay.

- Upload the **HC Exit Notice** under *Most recent inspection report*




Currently the only option to select to liaise with Health Canada is:
***Canada – Health Canada – manufacturer within Canada only***
This may be selected until the system is updated, as the manufacturing sites which require CV applications to be submitted are located outside of Canada

Please note: for MRA applications (where the manufacturer is located within Canada), only the Exit notice is required as evidence. This should be attached as the *current GMP Certificate* unless liaising for evidence is required. It should NOT be attached under *Most recent inspection report* as this is only for CV applications.

# Evidence

- Provide all supporting documentation as per the GMP Guidance.
- When submitting a variation – eg. increase of scope, sponsors still need to provide relevant evidence to support the application and pay all relevant fees. A sponsor can access their evidence that was previously submitted using a LOA.
- For both MRA and CV applications covering API(s), please provide an API declaration where required.

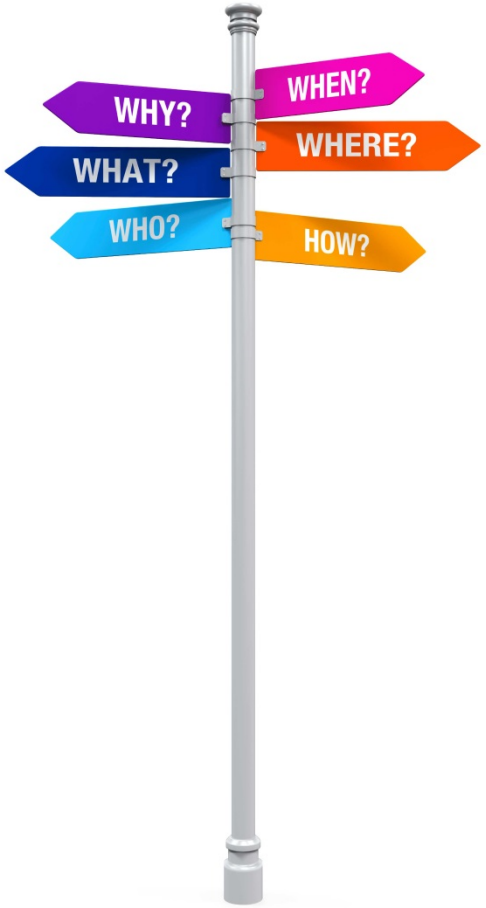
If you do not provide all required evidence your application will be delayed and the clearance may not be issued.

If you are not providing a document which is required by the Guidance, include appropriate justification in the application cover letter.

| 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

# Evidence: Cover letters




Cover letters should be used to provide additional clarification and information regarding the application purpose or scope, for example:

- Additional information regarding activities performed at the site
- Additional information regarding changes eg. updating manufacturer details
- Absence of evidence (where appropriate)
- Regulatory submissions – other applications that are related
- Overview of supply chain

# TGA certificates

- Where no supporting evidence is available or there are compliance issues for an overseas site, a TGA onsite inspection may be required.
- If you are a contributing sponsor to a TGA on-site inspection of an Overseas manufacturer, you do not need to submit another GMP clearance application.
- A GMP clearance will be issued to you following the issuance of the TGA certificate to the manufacturer.


If you decline to contribute to a TGA overseas inspection without reasonable justification, it is unlikely that a GMP clearance will be issued to you once the inspection is closed.

# Extensions

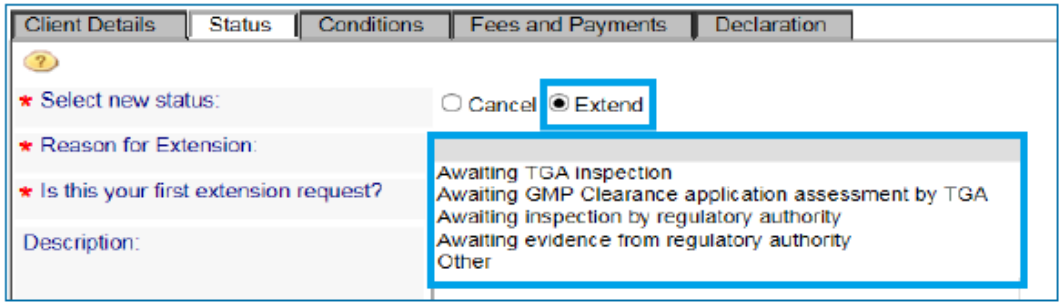
## Variation Applications

You may request a short term extension of your GMP clearance if there are valid reasons.

- Prior to submitting an extension request – check if there is any new GMP evidence available and if not investigate why.

If evidence is available submit a renewal application

- In ***Description*** include reason and explanation.
- Evidence may be required to support extension requests.
- If an extension is not granted and you cannot provide updated supporting evidence you may need to submit an application for a TGA on-site inspection.


- An extension request cannot be submitted via TGA Business Service portal after the clearance is expired for more than 30 days. You will need to contact GMPclearance@health.gov.au and a re-instatement fee will apply.

# Submitting an application – what to consider

What application type you are submitting? New or variation

| New Applications | Variation applications |
|---|---|
| • Manufacturer name | Purpose of the application:<br>• Renew<br>• Amend scope (increase or decrease)<br>• Extension<br>• Cancellation<br>• Change to manufacturer details (name/address)<br>• Change to sponsor or agent details |
| • Application scope: API or Finished product | |
| • Application scope:<br>Manufacturing Steps and<br>API names or dosage forms<br>Will the scope validate with the relevant regulatory submission system? | |
| • Is the application a CV application?<br>If it is, always select **YES** to the question:<br>Is this a Compliance Verification Assessment? | • Is the application a CV application?<br>If it is, always select **YES** to the question:<br>Is this a Compliance Verification Assessment? |
| • Is US FDA or Health Canada evidence submitted with a CV application? Yes<br>Then always select *'TGA to obtain GMP certificate'* | • Is US FDA or Health Canada evidence submitted with a CV application? Yes<br>Then always select *'TGA to obtain GMP certificate'* |
| • Does the supporting evidence cover the scope of the application?<br>• Is an API declaration required<br>• If using LOA to clearance or evidence, is the clearance or evidence scope equivalent or greater than the application scope? | • Does the supporting evidence cover the scope of the application?<br>• Is an API declaration required?<br>• If using LOA to clearance or evidence, is the clearance or evidence scope equivalent or greater than the application scope? |
| • Is the application complete (including supporting evidence) and have all of the required fees been paid? | • Is the application complete (including supporting evidence) and have all of the required fees been paid? |
| • Should a cover letter be provided? | • Should a cover letter be provided? |

# Website and link references

- Information about the GMP Clearance process is available at: https://www.tga.gov.au/publication/gmp-clearance-guidance
- Information about international agreements and arrangements for GMP clearance: https://www.tga.gov.au/international-agreements-and-arrangements-gmp-clearance
- Regular updates about changes are provided through the Notices about GMP Clearance webpage: https://www.tga.gov.au/notices-about-gmp-clearance
  - Increases to fees and charges
  - Timeframes
- Enquiries regarding desk top assessments using overseas regulator evidence: GMPClearance@health.gov.au
- Enquiries regarding general GMP enquiries, Australian manufacturers, overseas sites seeking a TGA inspection of their facility GMP@health.gov.au

Contact us

Manufacturing Quality Branch

Phone: 1800 020 653

Email GMPClearance@health.gov.au

Jodie Giess and Rheannon McNeil are currently reading over your submitted questions.

We'll be back shortly for **Q&A**

We appreciate your participation to complete our live poll.

# LIVE POLL

# Question time

# More information

GMP Clearance https://www.tga.gov.au/manufacturing-medicines

TGA website – www.tga.gov.au

Facebook – TGA Australia

Twitter – @TGAgovau

YouTube – TGA Australia

TGA topics blog - tga.gov.au/blogs/tga-topics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Therapeutic Goods Administration