Australian Government
Department of Health
Therapeutic Goods Administration

Remote GMP inspections:

Current Feedback and Future Considerations

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TGA Health Safety Regulation

Remote Inspections: current feedback and future considerations

- Scope
- Introduction of Remote Inspections
- GMP Inspection Process and Tips
- Current State
- Data and deficiencies overview
- International common issues and successes
- Future state

Scope:

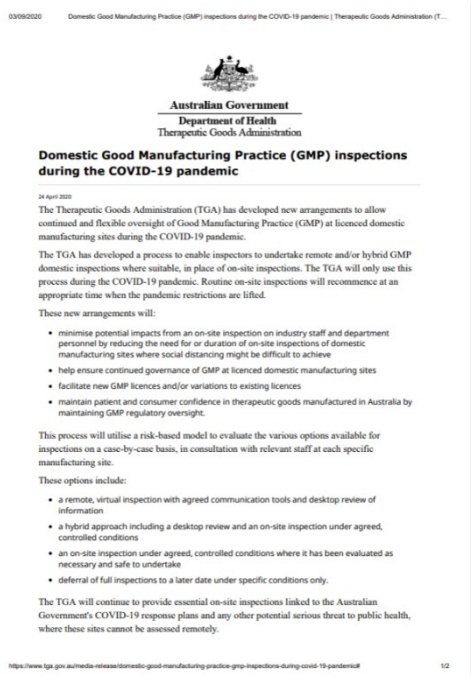
Includes inspections of manufacturers of therapeutic goods and blood and biologicals.

Excludes inspections of manufacturers of medical devices

Introduction of Remote Inspections

- The remote inspection process was introduced in March 2020 for domestic inspections and August 2020 for overseas inspections
- A series of web statements were also published

TGA GMP inspections during COVID-19



03/09/2020 Domestic Good Manufacturing Practice (GMP) inspections during the COVID-19 pandemic | Therapeutic Goods Administration (T...

Australian Government
Department of Health
Therapeutic Goods Administration

Domestic Good Manufacturing Practice (GMP) inspections during the COVID-19 pandemic

24 April 2020

The Therapeutic Goods Administration (TGA) has developed new arrangements to allow continued and flexible oversight of Good Manufacturing Practice (GMP) at licenced domestic manufacturing sites during the COVID-19 pandemic.

The TGA has developed a process to enable inspectors to undertake remote and/or hybrid GMP domestic inspections where suitable, in place of on-site inspections. The TGA will only use this process during the COVID-19 pandemic. Routine on-site inspections will recommence at an appropriate time when the pandemic restrictions are lifted.

These new arrangements will:

- minimise potential impacts from an on-site inspection on industry staff and department personnel by reducing the need for or duration of on-site inspections of domestic manufacturing sites where social distancing might be difficult to achieve
- help ensure continued governance of GMP at licenced domestic manufacturing sites
- facilitate new GMP licences and/or variations to existing licences
- maintain patient and consumer confidence in therapeutic goods manufactured in Australia by maintaining GMP regulatory oversight.

This process will utilise a risk-based model to evaluate the various options available for inspections on a case-by-case basis, in consultation with relevant staff at each specific manufacturing site.

These options include:

- a remote, virtual inspection with agreed communication tools and desktop review of information
- a hybrid approach including a desktop review and an on-site inspection under agreed, controlled conditions
- an on-site inspection under agreed, controlled conditions where it has been evaluated as necessary and safe to undertake
- deferral of full inspections to a later date under specific conditions only.

The TGA will continue to provide essential on-site inspections linked to the Australian Government's COVID-19 response plans and any other potential serious threat to public health, where these sites cannot be assessed remotely.

https://www.tga.gov.au/media-release/domestic-good-manufacturing-practice-gmp-inspections-during-covid-19-pandemic# 1/2

These new arrangements will:

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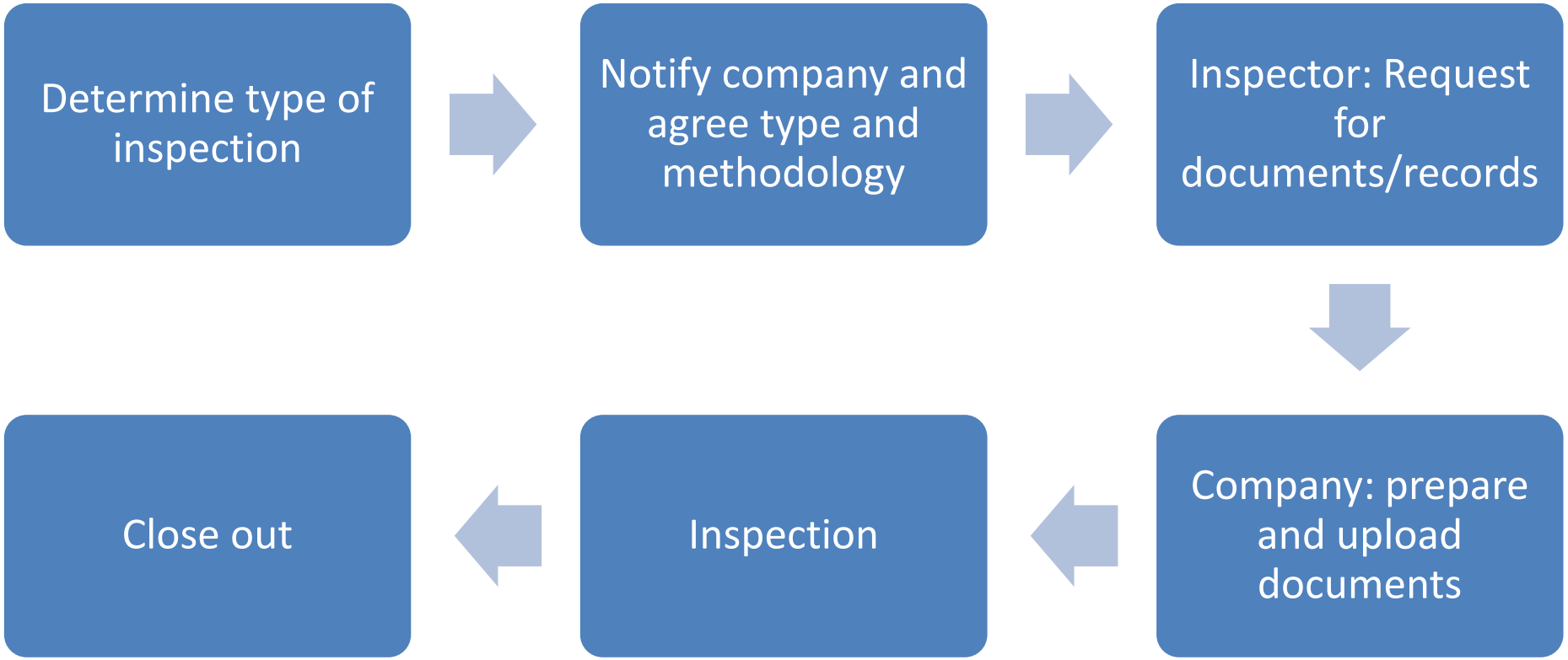
Process


Determine type of inspection
Notify company and agree type and methodology
Inspector: Request for documents/records
Company: prepare and upload documents
Inspection
Close out

Determine type of inspection

Criticality

- Manufacturing type (risk)
- Manufacturer's compliance history

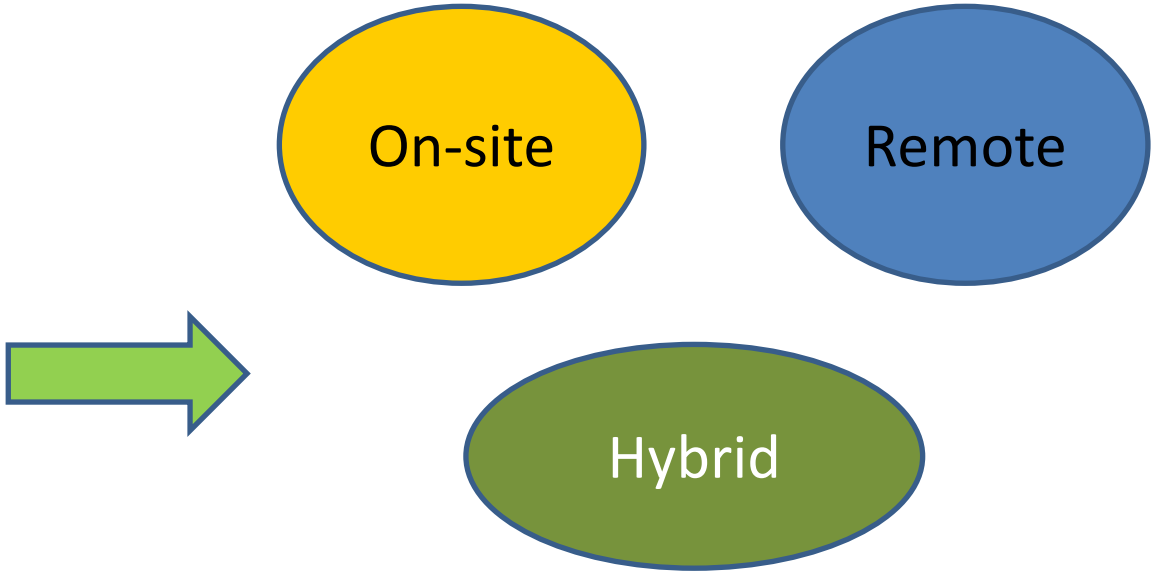
Protection of products a

- Manufacturer's int ments for protection of
- Manuf riction requirements for products
- rocedures for protection of inspectors

Tec logy

- Manufacturer's technological capability to support remote inspection

Federal, state and territory government restrictions and requirements where the manufacturer is located and where the inspectors are based

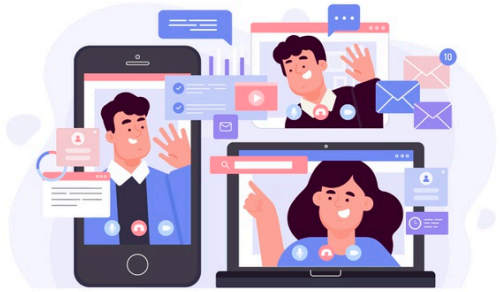


If deemed critical to be on-site, may delay that component until restrictions are lifted.

Inspection Methodology – Technology and limitations

Meeting

- Meeting apps; MS Teams and WebEx only (secured document repository)
- Phone if no other options



Document review

- Meeting apps for sharing of documents uploaded and documents on company's database
- Emails

Facility review

Live streaming using meeting apps, phone, tablet
Uploaded photos and pre-recorded videos

Availability of internet and size of bandwidth

Inspection process (1)

Scope

Default – same as if on-site

To be determined on a case by case basis

Inspection Methodology

Same as if on-site

Read documents, followed by Q&A

Length of Inspection

May take more days, but cumulative hours will be as if on-site

If major/critical non-compliance observed – duration may be more than originally planned or may include an on-site component at a later date.

Inspection process (2)

Response to deficiencies observed

No change to the process

Compliance level achieved

Will not be better than the previous (on-site) inspection

Can be lower than the previous (on-site) inspection

Tips (1)

Trial runs:
Test every individual device that will be used during the inspection

Trial runs:
Test every activity; send invitation, accept invitation, join the meeting, uploading/downloading of materials

IT support to troubleshoot problems during trial runs and remote inspection

Essential

Tips (2)

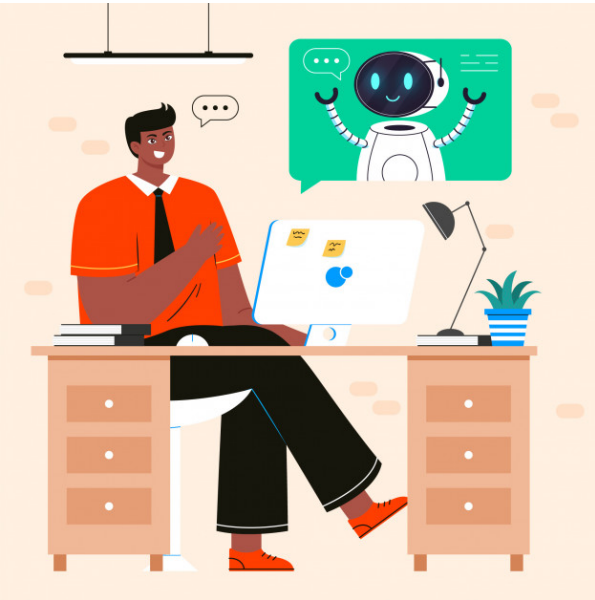
Documents/records for review:

- Sharing of uploaded documents
- Sharing of documents/records from company's database
- Use of accessorised camera for sharing documents
- Scanning of hard copy documents may be required
- Photos and videos may be required if live streaming is not available.

Uploaded documents:

- Logical file structure
- Logical naming convention for documents and files

Tips (3)



Presenters/SME's should:

- Know technology options to present
- Be conversant with the technology/app used – how to share documents from various sources

Please be aware of:

- Audio – mute/unmute, use of loud speaker (can cause echo)
- Video – on/off, background

Current status of inspection programs

Domestic Inspection Program
• No stoppage of inspections
• Reasonably up to date
• We have been conducting on-site, hybrid and remote inspections since March 2020

Overseas Inspection Program
• Inspection program interrupted since February 2020
• The first overseas inspection was carried out in August 2020
• Current backlog which is being addressed
• More challenges than domestic inspections; language, culture, time zone,
• Remote inspection only, no option of a hybrid or on-site inspection for the foreseeable future
• Looking at working with PIC/S member health authorities for their assistance if an on-site inspection component is required subject to them also being on site

Other considerations……

APVMA inspections	• No change. TGA continues to inspect on behalf of APVMA when required.

Licence vs GMP Certificate for Australian manufacturers	• Licence
	  • TGA issues a GMP licence to domestic manufacturer following a satisfactory initial inspection.
	  • Licence has no expiry date, and remains valid so long as the company accepts the TGA inspection when due and continues to be compliant.
	• GMP Certificate
	  • TGA issues a GMP certificate to domestic manufacturer based on the licence.
	  • GMP Certificate is valid for 3 years from the date of the last inspection.

Recognition of TGA remote inspections by other regulators	• GMP Certificate issued for domestic manufacturer includes a statement that the inspection was conducted remotely. • The destination country authority determines whether the inspection (and Certificate) is acceptable.

Current State

- TGA is currently performing remote, hybrid, on site inspections.
- The mode of inspection is based on the current situation with COVID in the state, manufacturer and inspector risk assessment, type of inspection and whether the mode would be adequate

Data on inspections- TGA

- For the period 1 March 2020 to 31 March 2021.
  - 130 remote domestic inspections
  - 148 onsite/hybrid domestic inspections
  - 37 remote overseas inspections

Deficiencies

- Complex deficiencies have been identified using remote inspections including “critical findings”.
- Deficiencies could be identified in an equivalently efficient way.
- Major observations have been identified and have seen a number related to documentation.
- Evaluation of data integrity issues can be difficult

International work

- A working group was established in mid 2020 to look at distant assessments internationally by ICMRA
- PICS seminar was held in December 2020 on distant assessments for PIC/S regulators sharing experiences
- Survey was performed for the PICS seminar in December 2020

Survey Data on Inspections- PIC/S

On-Site, Hybrid and Distant Assessments at the time of the Seminar

Domestic sites

- 69% of responders were able to conduct on-site inspections
- 57% were using distant assessment with virtual components
- 57% were using hybrid inspections

Foreign sites

- Only 14% of responders were performing on-site inspections
- 38% were using Distant Assessment with virtual components

Survey Data on Inspections- PIC/S

On-site, hybrid and distant assessments logistics

Video conference applications

- MS Teams and Webex were the most popular applications
- In 2/3 cases competent authority arranges the video conference

Verification of site location

- 29% of responders have used GPS

Verification of inspector identity

- 1/3 used showing of ID card by video to company being inspected

International initiatives

- Reflection paper on distant assessments is being drafted to be shared with regulators and industry by ICMRA
- PIC/S is also working with ICMRA collaboratively on this reflection paper
- Guidance written by EMA and other agencies

Common issues- internationally

Logistical

- Resource availability.
- Time zone differences.
- Inspections take longer.
- Translation between languages.
- Delays in receipt of requested documents.

Common issues- internationally

Logistical

- Inability to ask impromptu questions to subject matter experts.
- Inability to see facial expressions and body language.
- Inability to assess the state of premises, equipment and utilities.

Common issues- internationally

Logistical

- The lack of personal interaction whilst conducting remote inspections does not foster the development of trust, rapport
- Access to all electronic systems including management of accounts/passwords.

Common issues- internationally

Technology

- Web-based/digital interactions can have connection issues, inspections can be cancelled due to this.

- Remote interactions and document sharing impacted by site's technological capabilities.
- Not all inspections conducted using same file transfer systems.

Common issues- internationally

Technology

- Data privacy considerations.
- Audio troubles frequently occurred.
- The size of the electronic files shared and the time to download the file.

Remote inspection success

Regulatory considerations

- Allows more inspectors to participate and more documents to be reviewed.
- Facilitates theoretical training of new inspectors.
- Useful for follow up inspections.

Remote inspection success

Regulatory considerations

- Protects the health and safety of inspectors during times of risk.
- Reduces the travel costs associated with onsite inspections.
- Allows for more flexibility with the schedule of work for inspectors.

Remote inspection success

Industry considerations

- A remote inspection is better for applicants/sponsors than usual method because inspectors' questions were provided in advance.
- Sites appreciated the flexibility of remote inspections as it was less rigid and pressured than onsite.
- Protects the health and safety of the inspected party staff .

Remote inspection success

Industry considerations

- Reduces/eliminates the travel costs associated with onsite inspections for the industry quality team.
- Allows for more flexibility with the schedule of work for the regulated party personnel.
- A remote evaluation may also warrant delaying an on-site inspection, or justifying a reduction in depth and scope of an on-site inspection.

The future state- remote inspections

- The onsite inspection is the preferred mode of inspection
- Remote inspections may have a use in the future under controlled conditions
- The hybrid mode is preferred over the remote inspection

The future state- remote inspections

- Certain circumstances and activities are not suited to this format of inspection
- Consideration needs to be given on the acceptability of these inspections outside of emergency situations based on a risk assessment of the site

The future state- remote inspections

- From the shared experience and learning - remote inspections are possible using a combined / hybrid approach:
  - Desk Reviews
  - Live streaming of documents and processes
  - Teleconference and video conference including screen share
  - On site component

Future state- remote inspections- PIC/S

Future Plans When Pandemic Has Ended

- 28% of responders will continue to use remote inspection/distant assessment process for some activities
- 49% had not decided their post-pandemic plans yet
- Strong support for the development of guidelines and tools to harmonise procedures for distant assessments to facilitate continued reliance between international partners

The future state- remote inspections

Remote inspections may be considered for

- Some close out inspections
- Low risk manufacturing steps
- Some aspects of the inspection e.g. document review and other aspects are verified on site
- Not able to get to the manufacturing site

Conclusion

Remote inspection has limitations and cannot replace on-site inspection

More work is required to support a remote inspection (company and inspector). TGA will work flexibly with companies to enable inspections to be conducted as best the situation allows.

Remote inspections is being explored to be used in some controlled conditions in the future

Website and link references

Domestic inspections

Domestic Good Manufacturing Practice (GMP) inspections during the COVID-19 pandevic

Overseas inspection

TGA expectations for overseas manufacturing sites hosting remote inspections during the COVID-19 pandemic

Clearance

GMP Clearance questionnaire

A notice about the implications of adopting the PIC/S Guide to GMP PE009-14

Transition to new GMP requirements for medicinal products

Contacts:

General & Australian manufacturing enquiries: gmp@health.gov.au
Overseas manufacturing enquiries: gmpclearance@health.gov.au

Australian Government

Department of Health

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