FREQUENTLY ASKED QUESTIONS ON GOOD MANUFACTURING PRACTICE (GMP) AND GOOD DISTRIBUTION PRACTICE (GDP) INSPECTIONS BY NATIONAL PHARMACEUTICAL REGULATORY AGENCY (NPRA) DURING COVID-19 PANDEMIC

How does NPRA conduct GMP inspections during COVID-19 pandemic?

The Movement Control Order (MCO) was implemented under Prevention and Control of Infectious Diseases Act 1988 and Police Act 1967 commencing 1st March 2020. With reference to a letter issued by The Chief Secretary to the Government related to the control of infectious diseases (Ref: JPM.KSN.100-2/2/5Jld.3(52); dated 13th March 2020) and a letter related to restrictions on the Ministry of Health (MOH) employees to travel abroad (Ref: KKM.500-6/4/2 JLD 6(57); dated 5th March 2020), NPRA has decided to **suspend** all national and foreign GMP Inspections which has been scheduled for the year of 2020 until further announcement made by the government.

Subsequently, the government announced the implementation of Conditional Movement Control Order (CMCO) which was effective on the 4th May 2020 allowing most economic and social sector in the country to start operating with implementation of strict Standard Operating Procedure (SOP) set by the Ministry.

Due to this unprecedented situation, the following are NPRA's plan of action to conduct Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP) inspections that has been postponed since 18th March 2020.

The following are the frequently asked questions related to the management of GMP and GDP Inspections during the period of crisis for industry guidance;

A. NATIONAL GMP INSPECTIONS
B. FOREIGN GMP INSPECTIONS
C. GDP INSPECTIONS

A. NATIONAL GMP INSPECTIONS

1. Which manufacturers are involved in this revised inspection procedure?

Manufacturers involved in the manufacturing of to be registered/ registered products under Drug Control Authority (DCA) and to be notified/ notified cosmetics under NPRA.

2. What are the types of GMP inspections conducted by NPRA?

The types of inspections conducted by NPRA are:

(i) Routine GMP Inspection – GMP Inspection which has been scheduled for the current year.

(ii) Non-routine GMP Inspection which includes:

- Initial Inspection: Inspection conducted on new premises with an intention to manufacture notified cosmetics only.
- Pre-Licensing Inspection: Inspection conducted on new premises with an intention to manufacture registered products (such as pharmaceuticals, health supplements and traditional products).
- Pre-Approval Inspection: Inspection conducted on new production line of registered products/ notified cosmetics manufacturers
- Pre-Certification Inspection: Inspection conducted on local premises that are not regulated by Drug Control Authority such as foreign manufacturer, active pharmaceutical ingredient manufacturer and Cell and Gene Therapy Products (CGTP) manufacturer.
- Verification Inspection: Inspection conducted following a punitive action.
- Investigation Inspection: Investigation Inspection is an inspection conducted on premises based on complaint received and product recall activity.

Kindly refer to the Frequently Asked Questions (FAQs): Good Manufacturing Practice (GMP) Inspection by National Pharmaceutical Regulatory Agency (NPRA) for further information pertaining to the requirement of GMP.

3. How is GMP Inspection being conducted throughout COVID-19 pandemic in Malaysia?

Ideally, all routine and non-routine GMP inspections are conducted on-site whereby an inspector, or a team of inspectors will perform the inspection at the premises throughout the duration of inspection. Previously NPRA has implemented few off-site inspection mechanisms such as Desktop Inspection (DI), Desktop Assessment (DA) and Remote Inspection (RI). As a way forward, to improve the existing off-site inspection mechanisms, Distant Assessment (DiA) which comprises of Remote Inspection and Hybrid Inspection is introduced starting from 1st September 2021.

3.1 Remote Inspection

3.1.1 What is Remote Inspection?

Remote Inspection includes documentation review and followed by virtual inspection in which:

1. Documentation (e.g., filing commitments, site description, and key procedures) is requested by GMP inspectors for further evaluation. Requests and responses to questions are shared in written form (e.g., via email or on a document-sharing platform).

2. In addition to sharing documentation as in any other Remote Inspection, virtual inspections utilize technologies such as live or real-time streaming video, screen-sharing, or other means of real-time communication. Virtual inspections may include virtual tours of aspects of the manufacturer, video communications and interviews.

3.1.2 How does NPRA perform GMP inspection through Remote Inspection?

Below is the summary of Remote Inspection process:

1. The assigned GMP inspector(s) will communicate with the manufacturer on the arrangement of the inspection and the list of documents required for evaluation. The GMP inspector(s) in-charge may also forward invoice for inspection fee calculated based on the number of inspector/ assessors and the duration of the Remote Inspection days to be conducted.

   [Note: The full amount of inspection fee must be paid upfront before the GMP inspector(s) proceed with the process of Remote Inspection.]

2. The GMP inspector(s) will prepare the inspection/ document evaluation agenda based on inspection type.

3. The GMP inspector(s) will evaluate the documentation provided by the manufacturer.

4. The GMP inspector(s) may further communicate with the manufacturer's representative to request additional documents. Total correspondence with company shall be limited to 3 correspondences.

5. The GMP inspector(s) will notify company on the virtual inspection date. Virtual inspection will be conducted through an online platform according to the inspection agenda prepared by the GMP inspector(s).

   a) Opening Meeting.

   b) Outcome of documentation evaluation and further discussion/ document requested if it is deemed necessary.

   c) The manufacturer conducts a virtual tour on the facility.

   d) Closing Meeting.

6. An inspection report will be forwarded to the manufacturer.

7. The manufacturer is required to submit Corrective and Preventive Action Report (CAPA) based on the GMP deficiencies reported.

8. The GMP inspector(s) receives and evaluates CAPA report forwarded by the manufacturer.

3.1.3 What hardware is required or recommended for a virtual inspection?

The basic requirements for a virtual inspection follow:

1. Computer: All participants must have devices with a reliable internet connection of a speed that matches the requirements of the technological tools and communications platforms to be used.

2. Webcam or conference camera: A videoconferencing camera or a camera built-in to the computer can be used.

3. Audio: Computer audio must be suitable. The speakers and microphone for each participant should be of appropriate quality.

4. Intranet or virtual private network (VPN) connectivity at manufacturer: The manufacturer should test connectivity from all locations involved in the inspection, including those of key staff participating remotely, in advance of the start date to ensure that all software applications will be accessible.

5. Scanner can be helpful in all types of virtual inspections as the manufacturer prepares documents for sharing.

3.1.4 What is the most suitable process for sharing documentation in a Remote Inspection? In a virtual inspection, what is the most suitable process for conducting interviews and providing virtual tours of the facility?

All communication channels must be agreed by both parties and provide the appropriate level of protection for the exchange of confidential and sensitive information. Regardless of the technological tools selected, it is essential that all participants test and become familiar with the tools in advance of the inspection. In addition, access to document-sharing platform and virtual inspection platform should be revoked immediately 15 working days after inspection ends by the host (GMP inspector or manufacturer).

1. Sharing documentation

The manufacturer should prepare documents in digital format. Documents shared electronically should be:

a) Formatted to be as a readable Portable Document Format (PDF).

b) Provided in a clearly organized manner, consistent with the document request.

c) Identified in a way that enables the inspector to understand each document's contents from its title or file name without having to open the document.

d) The options for sharing documentation range from secured email to secured cloud storage solutions restricted to specific participants and made available only during the inspections.

e) If document-sharing platform is used, the platform should provide the appropriate level of security while also allowing auditors to easily locate, review, and annotate documents.

f) Documents also can be shared in real time during the virtual inspection through the video communication platform.

g) Documents also might be shipped through traditional mail or courier services, either in paper form or on electronic storage media.

h) The manufacturer should ensure that any electronic files are accessible by the inspector.

2. Virtual inspection

a) Video communication platforms can be used for many aspects of a virtual inspection, including video- and audio-conferencing and chat. Examples are Microsoft Teams, Cisco WebEx, and Zoom.

b) Care should be taken to ensure that the camera produces a stable picture that is easy to view.

c) Additional audio tools may be necessary for the person operating the camera during the virtual tour.

d) In areas of the facility where the Wi-Fi signal may not be strong enough to broadcast a live virtual tour, consider whether it might be useful to install devices to amplify the signal or prepare a pre-recorded video.

e) No recordings are allowed throughout the inspection process.

3.2 Hybrid Inspection

3.2.1 What is Hybrid Inspection?

Hybrid Inspection includes documentation review as described in para 3.1.1 (1) followed by on-site inspection. As most of the documents have been reviewed, time spent during on-site inspection can be shortened compared to normal on-site duration.

3.2.2 How does NPRA perform GMP inspection through Remote Inspection?

Below is the summary of Hybrid Inspection process:

1. The GMP inspector(s) in-charge will communicate with the manufacturer on the arrangement of the inspection and the list of documents required for evaluation. The GMP inspector(s) in-charge may also forward invoice for inspection fee calculated based on the number of inspector/ assessors and the duration of the Remote Inspection days to be conducted.

   [Note: The full amount of inspection fee must be paid upfront before the GMP inspector proceed with the process of Remote Inspection.]

2. The GMP inspector(s) will prepare the inspection/ document evaluation agenda based on inspection type.

3. The GMP inspector(s) will evaluate the documentation provided by the manufacturer.

4. The GMP inspector(s) may further communicate with the manufacturer's representative to request additional documents. Total correspondence with company shall be limited to 3 correspondences.

5. The GMP inspector(s) will notify company on the on-site inspection date. On-site inspection will be conducted according to the inspection agenda prepared by the GMP inspector(s).

   a) Opening Meeting.

   b) Outcome of documentation evaluation and further discussion/ document requested if it is deemed necessary.

   c) The manufacturer conducts on-site tour on the facility.

   d) Closing Meeting.

6. An inspection report will be forwarded to the manufacturer.

7. The manufacturer is required to submit Corrective and Preventive Action Report (CAPA) based on the GMP deficiencies reported.

8. The inspector(s) receives and evaluates CAPA report forwarded by the manufacturer.

3.2.3 What is the most suitable process for sharing documentation in a Hybrid Inspection?

Refer to para 3.1.4 (1).

3.2.4 What are the things to consider during on-site inspection (in the context of Hybrid Inspection)?

Steps that can be taken by both parties during on-site inspection to minimize the risk of transmission of infections are outlined as below but not limited to:

1. Reduce number of people in inspection/meeting room. Manufacturer may use video conference for people from other rooms to join inspection/meeting.

2. Reduce number of personnel accompanying during site tour.

3. Use screen sharing video conference technology in sharing documents.

4. If the outcome of the DiA is Acceptable, will a GMP certificate be issued?

GMP certificate will be issued upon application and the certificate shall specify type of DiA (Remote Inspection) conducted. The GMP validity for DiA shall be as follows:

4.1 Remote Inspection : 2 years

4.2 Hybrid Inspection : 3 years

5. What are the timelines to respond to documentation request?

The manufacturer is given 5 working days to provide feedback/ correspondence to documents requested. If additional time is needed, it should be discussed and agreed with the GMP inspector(s).

6. How GMP Inspector(s) determine which type of DiA applicable for the GMP inspection?

Selection for type of DiA is based on risk management principles in which complexity of premise, processes and products will be considered other than type of inspections and history of product complaints. The decision to determine type of DiA to be conducted on the site solely depends on the inspectors, based on the criterias set and risk assessment conducted.

For further enquiries/ information, kindly refer to:

Frequently Asked Questions (FAQs): Good Manufacturing Practice (GMP) Inspection through the following link https://www.npra.gov.my/index.php/en/faqs-compliance-and-licencing/faqs-gmp-inspection.html

B. FOREIGN GMP INSPECTIONS

1. What is the approach taken by NPRA in managing foreign GMP inspection that had been postponed during this COVID-19 pandemic?

NPRA have implemented mitigation plan for foreign GMP inspection scheduled for the year 2020 to ensure registration process (new registration and/or renewal) are uninterrupted.

Where possible, other pathways are being used to facilitate registration process for pending foreign GMP inspection applications including requesting additional information from applicants and existing inspection reports for facility that had been inspected by other competent authorities (e.g. Pharmaceutical Inspection Co-operation Scheme (PIC/S), ASEAN Listed Inspection Services).

Starting September 2021, Distant Assessment (DiA) which comprises of Remote Inspection will replace on-site foreign GMP inspection during COVID-19 pandemic when border closure/travel restrictions are in-place.

However, on-site foreign GMP inspection will be resumed once COVID-19 pandemic had subside. Product Registration Holder (PRH) will be informed from time to time regarding re-scheduling of affected foreign GMP inspections. Inspection will be prioritized based on the risk whereby all manufacturing facilities will be evaluated using risk-based approach to determine the need for on-site inspection.

2. How is GMP Inspection being conducted throughout the period of COVID-19 pandemic for foreign manufacturer?

Remote Inspection will be replacing on-site foreign GMP inspection starting from 1st September 2021.

2.1 What is Remote Inspection?

Remote Inspection includes documentation review and followed by virtual inspection in which:

2.1.1 Documentation (e.g., filing commitments, site description, and key procedures) is requested by GMP inspectors for further evaluation. Requests and responses to questions are shared in written form (e.g., via email or on a document-sharing platform).

2.1.2 In addition to sharing documentation as in any other Remote Inspection, virtual inspections utilize technologies such as live or real-time streaming video, screen-sharing, or other means of real-time communication. Virtual inspections may include virtual tours of aspects of the manufacturer, video communications and interviews.

2.2 How does NPRA perform GMP inspection through Remote Inspection?

Below is the summary of Remote Inspection process:

2.2.1 The GMP inspector(s) in-charge will communicate with the manufacturer on the arrangement of the inspection and the list of documents required for evaluation.

2.2.2 The GMP inspector(s) will prepare the inspection/ document evaluation agenda based on inspection type.

2.2.3 The GMP inspector(s) will evaluate the documentation provided by the manufacturer.

2.2.4 The GMP inspector(s) may further communicate with the manufacturer's representative to request additional documents. Total correspondence with company shall be limited to 3 correspondences.

2.2.5 The GMP inspector(s) will notify company on the virtual inspection date. Virtual inspection will be conducted through an online platform according to the inspection agenda prepared by the GMP inspector(s).

1. Opening Meeting.

2. Outcome of documentation evaluation and further discussion/ document requested if it is deemed necessary.

3. The manufacturer conducts a virtual tour on the facility.

4. Closing Meeting.

2.2.6 An inspection report will be forwarded to the manufacturer.

2.2.7 The manufacturer is required to submit Corrective and Preventive Action Report (CAPA) based on the GMP deficiencies reported.

2.2.8 The GMP inspector(s) receives and evaluates CAPA report forwarded by the manufacturer.

2.3 What hardware is required or recommended for a virtual inspection?

The basic requirements for a virtual inspection follow:

2.3.1 Computer: All participants must have a computer with a reliable internet connection of a speed that matches the requirements of the technological tools and communications platforms to be used.

2.3.2 Webcam or conference camera: A videoconferencing camera or a camera built-in to the computer can be used.

2.3.3 Audio: Computer audio must be suitable. The speakers and microphone for each participant should be of appropriate quality.

2.3.4 Intranet or virtual private network (VPN) connectivity at manufacturer: The manufacturer should test connectivity from all locations involved in the inspection, including those of key staff participating remotely, in advance of the start date to ensure that all software applications will be accessible.

2.3.5 Scanner can be helpful in all types of virtual inspections as the manufacturer prepares documents for sharing.

2.4 What is the most suitable process for sharing documentation in a Remote Inspection? In a virtual inspection, what is the most suitable process for conducting interviews and providing virtual tours of the facility?

All communication channels must be agreed by both parties and provide the appropriate level of protection for the exchange of confidential and sensitive information. Regardless of the technological tools selected, it is essential that all participants test and become familar with the tools in advance of the inspection. In addition, access to document-sharing platform and virtual inspection platform should be revoked immediately 15 working days after inspection ends by the host (GMP inspector or manufacturer).

2.4.1 <u>Sharing documentation</u>

The manufacturer should prepare documents in digital format. Documents shared electronically should be:

1. Formatted to be as a readable Portable Document Format (PDF).

2. Provided in a clearly organized manner, consistent with the document request.

3. Identified in a way that enables the inspector to understand each document's contents from its title or file name without having to open the document.

4. The options for sharing documentation range from secured email to secured cloud storage solutions restricted to specific participants and made available only during the inspections.

5. If document-sharing platform is used, the platform should provide the appropriate level of security while also allowing auditors to easily locate, review, and annotate documents.

6. Documents also can be shared in real time during the virtual inspection through the video communication platform.

7. Documents also might be shipped through traditional mail or courier services, either in paper form or on electronic storage media.

8. The manufacturer should ensure that any electronic files are accessible by the inspector.

2.4.2 Virtual inspection

1. Video communication platforms can be used for many aspects of a virtual inspection, including video- and audio-conferencing and chat. Examples are Microsoft Teams, Cisco WebEx, and Zoom.

2. Care should be taken to ensure that the camera produces a stable picture that is easy to view.

3. Additional audio tools may be necessary for the person operating the camera during the virtual tour.

4. In areas of the facility where the Wi-Fi signal may not be strong enough to broadcast a live virtual tour, consider whether it might be useful to install devices to amplify the signal or prepare a pre-recorded video.

5. No recordings are allowed throughout the inspection process.

3. If the outcome of the Remote Inspection is Acceptable, will a GMP certificate be issued?

GMP certificate will be issued upon application and the certificate shall specify type of DiA (Remote Inspection) conducted. The GMP validity for Remote Inspection is 2 years.

4. What are the timelines to respond to documentation request?

The manufacturer is given 5 working days to provide feedback/ correspondence to documents requested. If additional time is needed, it should be discussed and agreed with the GMP inspector(s).

5. Is there any change in foreign GMP inspection application submission flow due to COVID-19 pandemic?

The process of foreign GMP Inspection application is unchanged despite the pandemic. If PRH wish to put in application for any foreign GMP inspection, they can submit 'Borang Permohonan Pemeriksaan APB Luar Negara (BPFK-501)' along with processing fee of RM 5,000.00 to the GMP Section, CCQC.

6. Can PRH submit 'Borang Permohonan Pemeriksaan APB Luar Negara (BPFK-501)' for manufacturing facilities located in regions that are impacted by COVID-19 related travel restrictions?

Yes, application submission will not be impacted by COVID-19 travel restrictions. NPRA will inform involved PRH's on any updates from time to time.

7. What is the fee involve in Remote Inspection?

The payment structure for Remote Inspection consist of two parts, in which all shall be borne by the applicant as follows:

7.1 Processing Fee:

7.1.1 Payment of a processing fee of RM 5,000.00 upon application.

7.1.2 The processing fee is non-refundable.

7.2 Inspection Fee:

7.2.1 Payment of an inspection fee of RM 20,000.00 upon issuance of invoice by NPRA.

7.2.2 NPRA will issue an invoice to the company once inspection date is confirmed.

7.2.3 The payment shall be made using a banker's cheque payable to:

Name : BIRO PENGAWALAN FARMASEUTIKAL KEBANGSAAN/ AGENSI REGULATORI FARMASI NEGARA, KEMENTERIAN KESIHATAN MALAYSIA

7.2.4 The inspection fee is non-refundable under any circumstances.

For any further enquiries / information, kindly refer to:

Frequently Asked Questions (FAQs): Foreign Good Manufacturing Practice (GMP) Inspection through the following link https://www.npra.gov.my/index.php/en/faqs-compliance-and-licencing/faqs-gmp-inspection.html

C. GDP INSPECTION

1. Will the GDP inspection be conducted during the COVID-19 pandemic in Malaysia?

Yes, GDP inspection will be conducted on licensed importers / wholesalers either on-site (on-site) or remotely.

2. What are the differences between the above mentioned GDP inspection mechanisms?

The differences between the GDP inspection mechanism mentioned above are as follows:

Item	**Inspection Mechanism**	
	On-site	***Remote***
Method	Field inspection will be conducted on the premises.	Virtual inspection will be conducted on the premises.
Inspection scope	Please refer to Annex 2: General Points to Consider for Auditee in the current GDP Guideline.	
Preparation: **Before inspection**	● The company will be contacted by the inspector (via phone / email) to set the date of inspection. ● Documents pertaining to the GDP requirement must be prepared by the company and forwarded to the inspector before the inspection.	● The company will be contacted by the inspector (via phone / email) to set the date of inspection. ● Documents pertaining to the GDP requirement must be prepared by the company and forwarded to the inspector before the inspection. ● The company needs to familiarise with online communication applications such as Skype, Google Meet, etc. upon mutual agreement by both parties.
Preparation: **During inspection**	● Personal protective equipment such as 3-ply face mask and hand sanitiser should be provided at the premises during the inspection. ● The company must ensure that social distancing, good hygiene practice (frequent use of hand sanitiser / hand washing) are properly implemented and complied within the premises.	● The company will have to be ready at least 10-15 minutes before the inspection commencement using an agreed online communication application. ● The company must be prepared to move within the premises / store using communication equipment such as camera phones if requested by the inspector for verification purposes.

3. Is my company allowed to choose the mechanism for GDP inspection?

No, the mechanism for GDP inspection will be determined by NPRA based on defined criteria and its priority will be decided based on the risk of the premises and the products being distributed. The inspection mechanism will be notified to the company by the inspector prior to the inspection.

For any further enquiries / information, kindly refer to:

a. Frequently Asked Questions: Good Distribution Practice (GDP) through the following link https://www.npra.gov.my/index.php/en/faqs-compliance-and-licencing/faqs-gdp- inspection.html

b. Officers-on-duty via email: saeb@npra.gov.my