Sol-Gel
Advanced Topical Therapy

Case Studies: Remote Inspection

Date| Ness Ziona

CASE STUDIES:

- Pre-Approval Inspection (PAI)
- Bioresearch Monitoring Inspection (BIMO)

PRE-APPROVAL INSPECTION (PAI)

If travel restrictions prevent a pre-approval inspection, it's not an automatic complete response letter.

In situations where travel restrictions prevent FDA from conducting pre-approval inspections, the agency says it will not automatically issue a complete response letter for the application. Decisions related to an application will be based on the "totality of information available" to the agency.

The guidance document offers additional detail into what would likely happen if it's determined that an inspection is needed before approval of the application

Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers Guidance for Industry August 2020

FDA Inspection Records Request- Form 4003

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

FDA Inspection Records Request

Requesting Office Street Address	City	State	Zip Code
12420 Parklawn Drive	Rockville	MD	20857

To: Name of Individual	Title of Individual	Date of Request
[redacted]	[redacted]	09/04/2020

Firm Name [redacted]

Firm Street Address	City	State	Zip Code
[redacted]	[redacted]	[redacted]	[redacted]

Country [redacted]

Under section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 371(a)(4)], FDA requests that you provide the records described below. If the records requested do not exist, please state that fact in your response.

DESCRIPTION OF RECORDS REQUESTED
See Attached List

Please submit the above-described records by email to the contact email below by **(Date)** 09/14/2020 . If you are unable to send via email and would rather send via mail, please contact the FDA contact email below.

FDA Inspection Records Request

#	Request
1.1	Site Master File (SMF) (English version if available): Provide a copy of your Site Master File document.
1.2	Point of Contact information: name/title, mailing address, phone, email address, fax, relation to Most Responsible Person at the site. The name and contact information of your US agent.
1.3	Major changes in the last 3 years or since the previous FDA inspection, whichever is less (organization, operations, facilities/ equipment)
1.4	Documentation records showing corrections made by your firm regarding previous FDA Inspectional Observations, FDA 483.
1.5	Provide a copy of the following procedures: a. Out of Specifications b. Deviations c. Investigations d. Training, change control e. Manual integration f. Review of raw data, g. All procedures considered to be data integrity procedures.

FDA Inspection Records Request

1.6	Provide the following written procedures in support of [redacted], [redacted] a. Receiving, testing release and packaging of raw materials, drug substance, in-process materials and finished product b. Vendor/supplier qualification practices. c. Provide a summary of the most recent supplier qualification.
1.7	a. Provide a facility diagram labeled with processing areas/rooms and operations for [redacted], along with photos of the major manufacturing equipment. Annotate the diagram with room numbers and locations of equipment including equipment name and number.

Additional request for information

- **Provide a facility diagram labeled with processing areas/rooms and operations for XXX along with photos of the major manufacturing equipment. Annotate the diagram with room numbers and locations of equipment including equipment name and number.**
- **Provide your Purified Water System written procedures including monitoring, prevention maintenance, sanitization, etc**
- **Provide commercial manufacturing equipment used in each manufacturing stage for XXX This includes Maker/Manufacturer, Model #, Capacity/Volume, and its respective working range, equipment ID#, Installation and qualification dates**
- **Indicate if these pieces of equipment are shared or dedicated equipment. If it is shared equipment, provide the products for which they share, along updated SOP and cleaning validation documents including the current protocol and report. Refer to Observation 4 issued in FDA Form 483 during inspection conducted in Oct 2019 for cleaning procedures for the equipment used in the formulation of liquid drug products.**

Additional request for information

- Provide the qualification protocol and summary reports (i.e., installation, operational, and performance qualification) for the Packaging Machine Provide photos or video of this unit of operation with time stem to include the different sequences occurring during the manufacturing process.
- Provide written procedures for the following items:
  - Operation of Packaging Machine
  - Handling and cleaning procedures of product filling hoses and nozzles
  - Cleaning procedures of the filing line
  - Handling procedures of packaging components

Additional request for information

- A list of all batches of XXX manufactured which were not in ANDA (if any), including any development batches that were rejected and validation batches, if applicable. Please include the batch number, date of manufacture, batch size, and purpose of the batch. Include batches for all purposes to include but not limited to development, R&D, exhibit, stability, clinical, scale up, and registration. If batches were rejected, please include the reason for the rejection.
- For all batches of XXX listed in ANDA and above list in request 1.10, provide a tabulated list of all manufacturing deviations (planned or unplanned), equipment deviations, or any other non-conformance associated with manufacture of the batch. Include the date of occurrence, the impacted batch, the date of investigation initiation, date of closure, a summary of the incident, a summary of the resolution of the incident, root cause, and associated CAPA if applicable.

Additional request for information

- For all batches of XXX listed in ANDA and above list provide a tabulated list of all out of specification (OOS) analytical results including in-process, release, and stability tests (confirmed or unconfirmed). Include the impacted batch, nature of the OOS, summary of the investigation, impact assessment, and conclusion.

- Please include a list of all analytical results for XXX listed in ANDA derived from manually integrated chromatograms and indicate why manual integration was performed. Further, provide copies of the unprocessed and processed chromatograms, if applicable.

Additional request for information

- **If available, provide both the manufacturing validation protocol and report pertaining to release of the process performance qualification batches of XXX**
- **Provide a listing of the equipment in the laboratory used for release and stability testing of XXX Include the equipment identification number and date of qualification for most recent requalification and calibration, and dates used for testing and sampling log.**
- **Please provide raw data for the microbial testing limits of the exhibit batches of XXX (this may include laboratory notebooks, worksheets, etc.) and indicate how these data are impacted by Observations 6 and 7 issued in FDA Form 483 of the inspection conducted in Oct 2019.**

Additional request for information

- **Please provide photocopies of the notebook pages/data packages supporting Report R/AT/GN080/003 associated with system suitability, specificity, precision, linearity/range, and accuracy of the HPLC method used for Assay in developing the subject drug product. If not already in the data packages, please provide sample set sequence list, along with all chromatograms injected.**

- **In a separate PDF file, please provide two different views of chromatograms including injection details and integration results table for all injections, full view, and Y-axis zoomed in (Max 0.5mAu, Min -0.2mAu) and X-axis full 0-10 mins.**

- **In addition, provide audit trail for the sample set and sample sequence.**

BIORESEARCH MONITORING INSPECTION (BIMO)

Similarly, the need for and selection of sites for BIMO inspections will continue to be risk-based, considering application and site-specific factors.

Manufacturing, Supply Chain, and Drug and Biological Product Inspections During COVID-19 Public Health Emergency Questions and Answers Guidance for Industry August 2020

BIMO remount audit at CRO

- Provide a copy of study monitoring plan, monitoring list, dates and list of observations.
- Provide the corrective actions as were reported by the investigators.
- Study timeline including FDA and IRB approval, study initiation etc.
- Provide site selection procedure.
- Provide site qualification procedure.
- Provide deviations handling procedure.
- Provide safety event review procedure.


Good Luck!