# APPLICATION-RELATED INSPECTIONS

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#### AGENDA



- FDA Inspection Authority
- Types of Application-Related Inspections
- What to Provide in an Application to Prepare for an Inspection
- What to Expect Before an Inspection
- Inspection Objectives
- Initiating an Inspection
- Inspection Close-out
- Resources

#### FDA INSPECTION AUTHORITY



#### Section 704(a) of the FD&C Act:

- Factories, warehouses, establishments, vehicles.
- All pertinent equipment, finished and unfinished materials, containers, and labeling.

### Inspections are performed by:

- Office of Regulatory Affairs (ORA)
  - Tobacco Operations Staff
- Center for Tobacco Products (CTP)
  - Representatives from the Office of Compliance & Enforcement (OCE)

# TYPES OF APPLICATION-RELATED INSPECTIONS



#### Manufacturing (Establishment) Inspections:

- Establishments associated with the manufacture, testing, or storage of the tobacco product(s) subject of the application(s) submitted to the Agency.
- · Should be inspection-ready at the time of application submission.

### Bioresearch Monitoring (BIMO) Inspections:

 Sites and entities associated with clinical and nonclinical studies submitted in support of the premarket application(s) submitted to the Agency.

#### Inspections may be performed domestically or internationally.

 Form FDA 482, Notice of Inspection will be issued during domestic inspections.

## WHAT TO PROVIDE IN AN APPLICATION TO PREPARE FOR AN INSPECTION



#### Manufacturing Inspections:

- A full description of each manufacturing and testing facility:
  - Address, point of contact, and assigned Firm Establishment Identifier (FEI) number.
  - A full description of all manufacturing and testing activities, processes, and controls performed at each facility.
  - A narrative description, accompanied by a list and summary of all standard operating procedures (SOPs).
  - If available, production schedule(s) for each of the final manufactured products subject to the application(s) for the first four months after the dates of the submission of your application(s).

## WHAT TO PROVIDE IN AN APPLICATION TO PREPARE FOR AN INSPECTION



### Bioresearch Monitoring:

- List of all clinical / nonclinical studies submitted in support of an application.
- List of all sites and investigators that conducted the study.
- All versions of protocols and amendments that were used in the study.
- Line data.
- Location of all source data.
- List of all contractors who participated in the study.
- Full report of all findings.

## WHAT TO PROVIDE IN AN APPLICATION TO PREPARE FOR AN INSPECTION



### Bioresearch Monitoring:

- Documentation of all actions taken to ensure the reliability of the study data and protection of human subjects.
- All versions of study materials.
- All versions of case report forms.
- Individual subject case report forms.

# WHAT TO EXPECT BEFORE AN APPLICATION-RELATED INSPECTION



#### **Pre-Inspection Notification:**

- Manufacturing Inspection(s)
- BIMO Inspection(s)

### Purpose of Pre-announcing:

- To notify the applicant/sponsor/investigator what sites are planned for inspection.
- To provide information to prepare the appropriate documentation for the inspection.
- Note that documents other than what was requested in the inspection pre-announcement may be requested during the inspection.

### INSPECTION OBJECTIVES



- Review processes and procedures.
- Observe and evaluate operations (manufacturing only).
- Document and collect information.
- Identify violations.
- Communicate potential violations to firm management.
- Document any proposed corrective action plans.

### INITIATING AN INSPECTION



- Meet with most responsible person on site.
- Present FDA credentials.
- Issue Form FDA 482, Notice of Inspection.
  - domestic inspections only.

# WHAT IS COVERED DURING AN APPLICATION-RELATED INSPECTION



Manufacturer Inspection	BIMO Inspection
Administrative information	Human subject protection
<ul> <li>Facility walk-through</li> </ul>	<ul> <li>Protocol compliance</li> </ul>
Observe the manufacturing	Data audit
process	
<ul> <li>Review of packaging, labeling,</li> </ul>	
and advertising	

#### INSPECTION CLOSE-OUT



#### What happens:

- Close-Out discussion.
- Discuss observations with management.
- Issue Form FDA 483, if necessary.
- Solicit firm's responses to observations.

#### INSPECTIONS – FINAL REPORT



### Establishment Inspection Report (EIR):

Describes the information discussed and collected during the inspection.

#### Field Management Directive 145:

- Copy of EIR to inspected entity.
  - Sent to most responsible individual identified during the inspection after decision has been made on the application(s).

## FDA RESOURCES AND CONTACT INFORMATION



#### CTP Website:

http://www.fda.gov/TobaccoProducts/default.htm

#### **CTP Webinars:**

• https://www.fda.gov/tobaccoproducts/guidancecomplianceregulatoryinformation/ucm220111.htm

#### For General Inquiries, contact via email or phone:

- AskCTP@fda.hhs.gov
- 1-877-CTP-1373

#### Sign up for updates:

• <a href="https://www.fda.gov/tobacco-products/ctp-newsroom/sign-email-updates-ctp">https://www.fda.gov/tobacco-products/ctp-newsroom/sign-email-updates-ctp</a>

#### Investigations Operations Manual (IOM):

• https://www.fda.gov/iceci/inspections/iom/default.htm

#### Regulations: Good Clinical Practice and Clinical Trials:

https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/regulations-good-clinical-practice-and-clinical-trials
 trials

#### Reporting Complaints Related to FDA-Regulated Clinical Trials:

• <a href="https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/reporting-complaints-related-fda-regulated-clinical-trials">https://www.fda.gov/science-research/clinical-trials-and-human-subject-protection/reporting-complaints-related-fda-regulated-clinical-trials</a>