What to Expect on FDA Inspections

Tania Hall
Investigator / Biologics National Expert
Office of Biological Products Operations
Office of Medical Products & Tobacco Operations
Office of Regulatory Affairs

September 29, 2020

Objectives

- Describe the FDA inspection
- Help you, a reproductive HCT/P establishment, prepare for an FDA inspection
- Provide tips to promote a smooth inspection

What is an FDA Inspection?

- We call it an “EI” or establishment inspection.
- Inspections are careful, critical, official examinations of a facility to determine its compliance with the laws enforced by FDA.
- Reproductive establishments are subject to the Public Health Service (PHS) Act and associated regulations.

Inspection Frequency

- There is no statutory requirement for FDA to conduct routine biennial EIs of reproductive establishments
- Office of Regulatory Affairs (ORA), Office of Biological Products Operations (OBPO) identifies which firms to inspect based on:
  - The firm's history of compliance, especially those with a non-compliant last EI
  - Establishments for which FDA has received information of potential violations of the regulations
  - Facilities that are newly registered and have been in operation for at least 1 year

Will I know You're Coming?

- FDA inspections are generally unannounced, with a few exceptions.
- Inspections of reproductive firms are not pre-announced.
  - However, during the COVID-19 Pandemic, we are pre-announcing in order to adhere to safety and social distancing recommendations.

We Love Having You Here…But How Long Are You Staying?

- Inspection length will depend on the operations performed, size of firm, availability and ease of review for records and procedures, number/type of issues and complexity of the issues found.

What Happens First?

- Investigator(s) will identify themselves and ask to see the most responsible individual (MRI) available at the time the inspection begins.
- FDA credentials will be displayed and form FDA 482, Notice of Inspection, will be issued to the MRI available.
- An FDA Contact Information Sheet will also be provided at some point during the inspection.
- Investigator(s) will explain the purpose of the “visit”.
  - In general, this will be to conduct an inspection and assess compliance with regulation(s).

Inspection Anatomy

- Standard Operating Procedure (SOP) review
- Manufacturing record review:
  - For reproductive firms this includes recovery, donor screening, donor testing, donor eligibility determinations, storage, quarantine, labeling, and distribution (i.e. transfer).
- Evaluate if your SOPs reflect what you're actually doing and whether your records and SOPs meet requirements in the regulations (21 CFR 1271).
- Deficiencies may or may not become observations listed on Form FDA 483.

Routine Inspection Requests

- Specific data will be requested over a set time range, such as since the last EI, and will include:
  - How many anonymous, directed, autologous donors, and Sexually Intimate Partners (SIP) clients were recovered
  - How many surrogates were used (with and w/o SIPs)
- Information about in-house oocyte, semen, and/or surrogate programs and from where else donors are obtained (i.e. donor agencies).
- Information about the testing lab that performs donor testing and specifics about testing.

How Can I Prepare in Advance?

- Know where to find the HCT/P Compliance Program

  https://www.fda.gov/vaccines-blood-biologics/enforcement-actions-cber/compliance-programs-cber

- Know where to find HCT/P Guidance Documents that apply to reproductive firms

  https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/tissue-guidances

- Know where to find the appropriate test kits for HCT/P Donor Communicable Disease Testing

  https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/testing-human-cells-tissues-and-cellular-and-tissue-based-product-hctp-donors-relevant-communicable#approved

How To Facilitate An Inspection

- Recommend designating one or more persons to facilitate the following during an inspection:
  - Requested SOPs and records are retrieved
  - Documents are photocopied as requested
  - Employees with the necessary knowledge or information are identified and made available.
- Recommend keeping an updated hardcopy of current SOPs or at least a table of contents (this provides easy access for review).

Promoting a Smooth Inspection

- Don’t be afraid to ask questions, this will help avoid miscommunication.
- Ask for clarification because you might use different terminology than we do.
- If you don’t know the answer to a question, find the person who does.
- Provide requested records as soon as possible or explain why there is a delay. (e.g., Those records are stored off-site and may take a day to retrieve.) Open communication is best.

Promoting a Smooth Inspection (Continued)

- Expect investigators to ask questions of the employees that actually perform the work.
- If more than one investigator is on inspection, expect they will need time alone to discuss amongst themselves.
- At the end of each day, ask the investigator what he/she covered and if there are any deficiencies.
- Understand deficiencies may or may not become observations listed on Form FDA 483.

The Inspection is Over ☺…Now What?

- The investigator(s) will have a closing meeting with, at minimum, the most responsible individual present.
- If objectionable conditions, deviations, and/or deficiencies were found, a Form FDA 483, Inspectional Observations, might be issued (☹).

Form FDA 483, Inspectional Observations

- Observations are made by the FDA investigator(s) during the EI.
- In the experience, judgment, and knowledge of the FDA investigator(s), the observations are potential violations of FDA regulations.
- The observations cited do not represent the final Agency determination regarding compliance.

Discussion Items

- The FDA investigator(s) may bring up issues of concern that are not placed on a Form FDA 483.
- These “discussion items” will be included in the narrative Establishment Inspection Report (EIR).

Responding To A Form FDA 483

- It is encouraged, but not required, to respond to Form FDA 483 in writing.
- Written responses can be sent via email to: orabioinspectionalcorrespondence@fda.hhs.gov
- If you choose to respond in writing, do so within 15 business days so your responses can be taken into consideration if any compliance action is being decided upon.

Public Access to FDA CBER

CBER website:

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

Consumer Affairs Branch (CAB)

Email: ocod@fda.hhs.gov

Phone: 800-835-4709 or 240-402-8010

Manufacturers Assistance and Technical Training Branch (MATTB)

Email: industry.biologics@fda.gov

Phone: 240-402-7800

Follow us on Twitter

https://www.twitter.com/fdacber

How to Engage With FDA ORA

- **Who do I contact following my FDA inspection?**
  - E-mail your inspection-related correspondence to orabioinspectionalcorrespondence@fda.hhs.gov
  - Electronic responses are preferred.
  - If responding via mail, send hard copy responses to the address listed in the upper right-hand corner of your Form FDA 482 (Notice of Inspection), which was issued at the start of the inspection.
- **What other contact information might I need?**
  - The Program Division Director (PDD) supervises all inspections and compliance activities.
    - Elizabeth Waltrip (Division 1) - Elizabeth.Waltrip@fda.hhs.gov
    - Karlton Watson (Division 2) – Karlton.Watson@fda.hhs.gov

How to Engage with FDA ORA (Continued)

- **What other contact information might I need?**
  - The Director of Investigations Branch (DIB) manages all inspectional activities.
    - Lisa Harlan (Division 1) – Lisa.Harlan@fda.hhs.gov
    - Tricia Samaniego Martinez (Division 2) – Tricia.Martinez@fda.hhs.gov
  - The Director of Compliance Branch (DCB) manages Form FDA 483 responses and post-inspection compliance activities.
    - Julie Bringger (Division 1) – Julie.Bringger@fda.hhs.gov
    - Catherine Quinlan (Division 2) – Catherine.Quinlan@fda.hhs.gov


FDA
U.S. FOOD & DRUG
ADMINISTRATION