Navigating FDA Inspections: Best Practices and Lessons Learned

Early Career Faculty Leadership & Training Lecture Series

October 30, 2024

FDA inspection basics

FDA Bioresearch Monitoring (BIMO) Program Objectives

- Protect subject rights, safety, and welfare.
- Assure quality, reliability, and integrity of clinical trial data.
- Assess compliance with FDA regulations.

BIMO Clinical Investigator Inspections

- Surveillance or application-based: verify conduct of study and data submitted with a sponsor's commercial application to FDA.
- For cause: generally in response to safety concerns, suspected or reported noncompliance, or complaint received by FDA.

What an FDA inspection is **not**

Joint Commission or DOH Survey

- Assessment of a clinical facility; includes operations, physical locations, and free-range interviews
- Unannounced, but usually occur at specified intervals
- Large team of surveyors
- Fred Hutch team: Accreditation and Regulatory Affairs
- High stakes for institution and clinic leadership

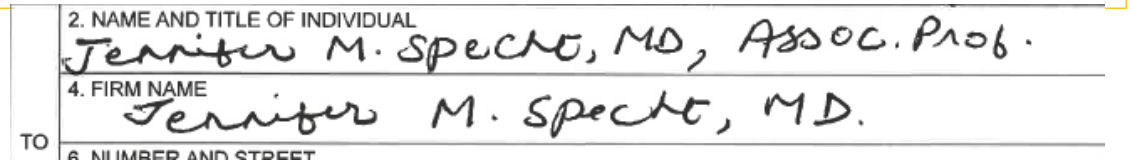
NCTN, Cooperative Group, or NCI Audit

- Assessment of multiple protocols under the program (may involve > 1 protocol PI)
- Announced several weeks in advance with protocols and subjects
- Small team of auditors
- Fred Hutch team: Clinical Research Support – NCTN
- High stakes for program leadership, institution, and study PIs

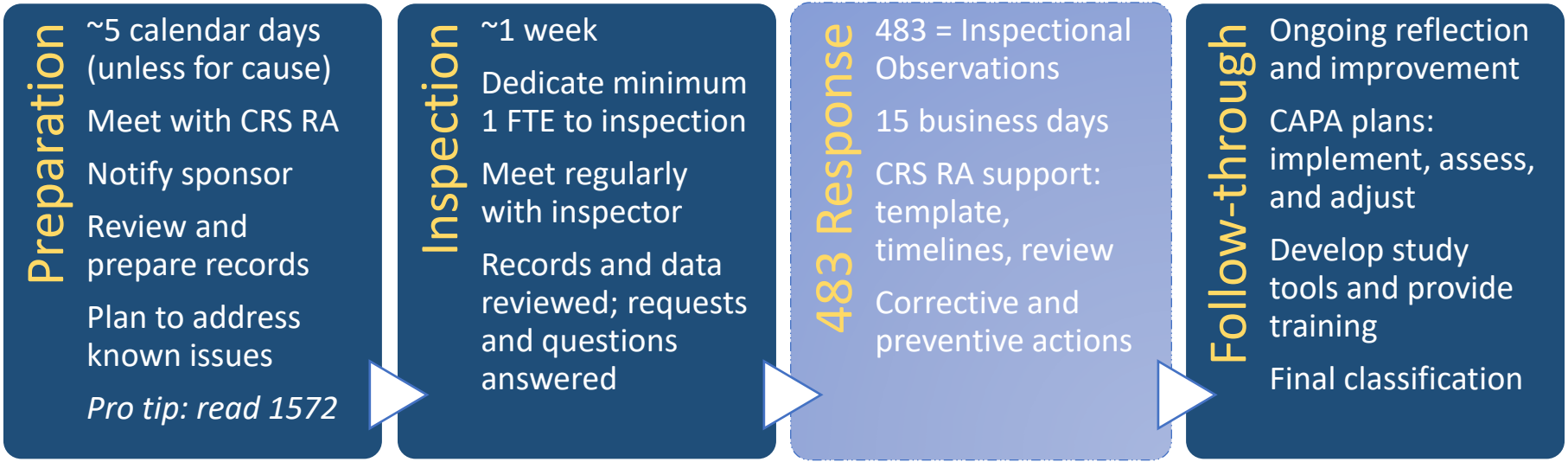
What an FDA inspection **is**

FDA BIMO Clinical Investigator Inspection

- Assessment of a PI's conduct of a study, primarily via document/data review and interviews
- Typically announced ~5 calendar days in advance; may be unannounced
- One inspector (rarely two)
- Fred Hutch team: Clinical Research Support – Regulatory Affairs
- High stakes for PI
  - ➢ Institution and Sponsor-Applicant also impacted


TO
2. NAME AND TITLE OF INDIVIDUAL
Jennifer M. Specht, MD, Assoc. Prof.
4. FIRM NAME
Jennifer M. Specht, MD.
6. NUMBER AND STREET

FDA inspection lifecycle



Inspection outcomes and classifications

After the inspection

- FDA investigator submits Establishment Inspection Report (EIR).
- PI submits 483 response, if inspectional observations were issued.
- Center that assigned inspection (CDER, CBER, or CDRH) reviews EIR and PI's response to determine classification.

Classifications

- No Action Indicated (NAI)
- Voluntary Action Indicated (VAI)
- Official Action Indicated (OAI): may result in Warning Letter

Insufficient response to a 483 or warning letter may lead to more significant FDA actions.

Guest Panelists

Mazyar Shadman, MD

- March 2022
- Zanubrutinib in CLL/SLL (approved 2023)
- No 483; NAI classification
- *Inspection readiness*

Jennifer Specht, MD

- August 2020
- Adjuvant treatment with pembrolizumab for TNBC (approved 2021)
- No 483; NAI classification
- *Inspection conduct*

Heidi Gray, MD

- November 2018
- “Legacy” GOG trial (2012; HG became PI 2014)
- For-cause: protocol deviation at outside site
- 483; VAI classification
- *Inspection follow-up*

Thank you for attending

Resources

- Hutch Learning Modules: FDA Inspections – Before the Event, During the Event, and After the Event
- Clinical Research Support FDA Inspection Guidelines (CRRW)
  https://fredhutch.sharepoint.com/sites/CRRWSPO/FormsTemplates/FDA%20Inspection%20Guidelines.pdf
- Sample FDA inspection questions (CRRW)
  https://fredhutch.sharepoint.com/:b:/r/sites/CRRWSPO/Study%20Tools%20Library/Sample%20FDA%20Inspection%20Questions.pdf?csf=1&web=1

- FDA Compliance Program: Bioresearch Monitoring of Clinical Investigators and Sponsor-Investigators
  https://www.fda.gov/media/75927/download
- FDA Information Sheet Guidance: FDA Inspections of Clinical Investigators https://www.fda.gov/media/75185/download
- FDA Clinical Investigator Training Course (CITC) – Virtual Conference December 10-12, 2024
  https://www.fda.gov/drugs/news-events-human-drugs/fda-clinical-investigator-training-course-citc-2024-12102024
- Clinical Investigator Site Inspections – What to Expect (slides from FDA CITC 2023)
  https://www.fda.gov/media/175400/download?attachment

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