Center for Drug Evaluation and Research (CDER) Bioresearch Monitoring (BIMO) Program – A General Overview

Kelly M. K. Nolen, Ph.D.
Compliance Reviewer, Compliance Enforcement Branch
Division of Enforcement and Postmarketing Safety
Office of Scientific Investigations/Office of Compliance
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

CDER BIMO Good Clinical Practices (GCP) Compliance and Enforcement – February 16, 2022

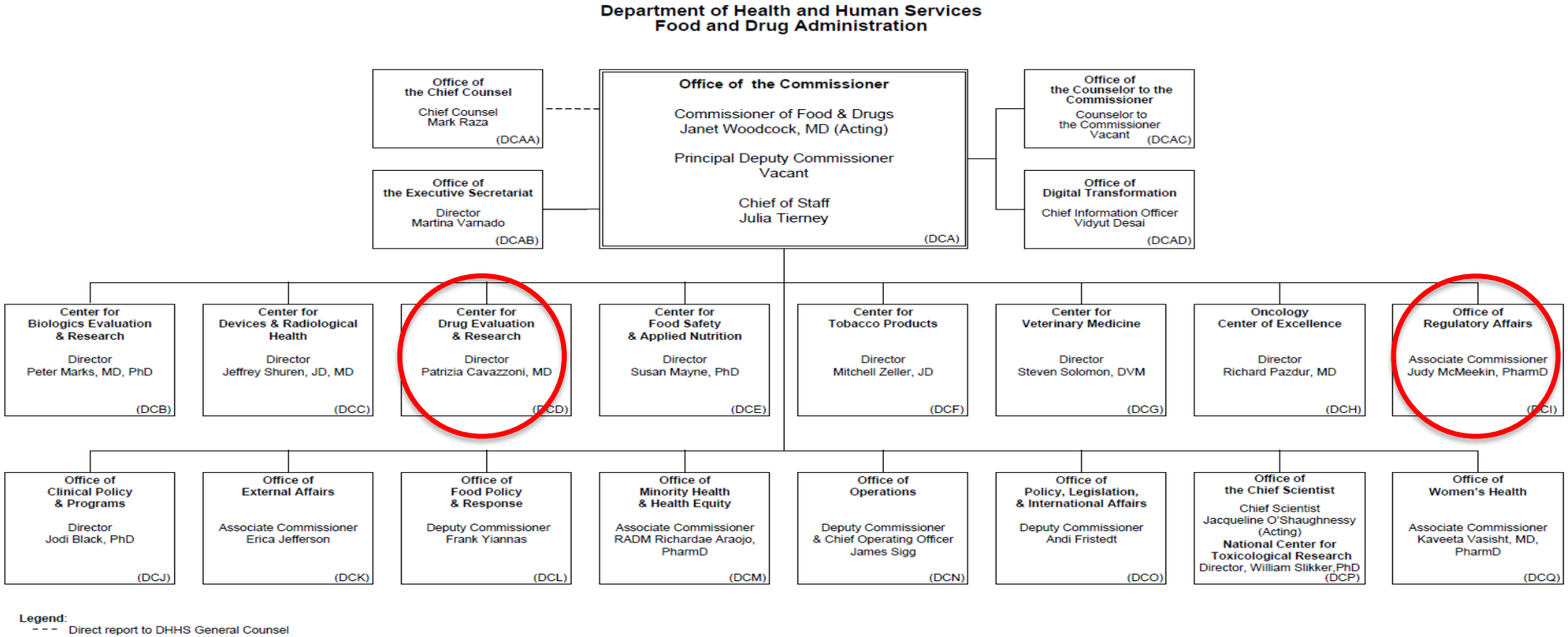
Disclaimer

The contents of this presentation are my own and do not necessarily reflect the views and/or policies of the Food and Drug Administration or its staff as per 21 CFR 10.85(k).

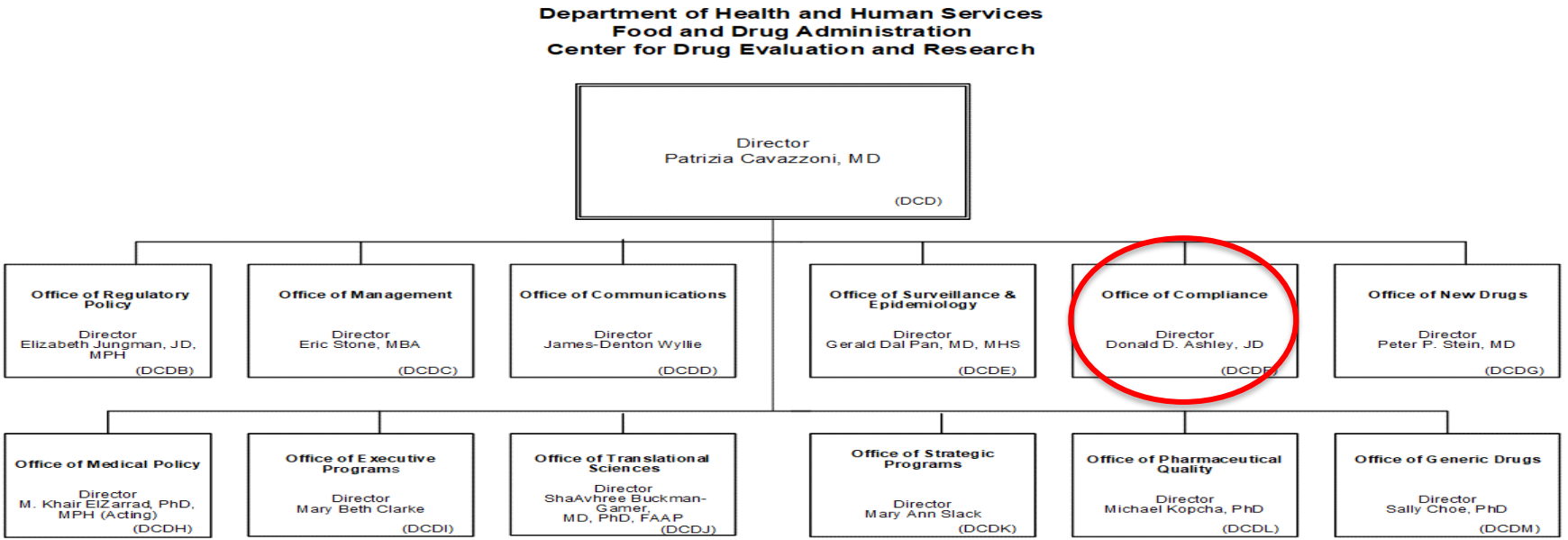
Overview

- CDER's BIMO program
- Good Clinical Practice (GCP) inspections under BIMO
- CDER BIMO inspections and related activities
- Recent trends in BIMO compliance and enforcement

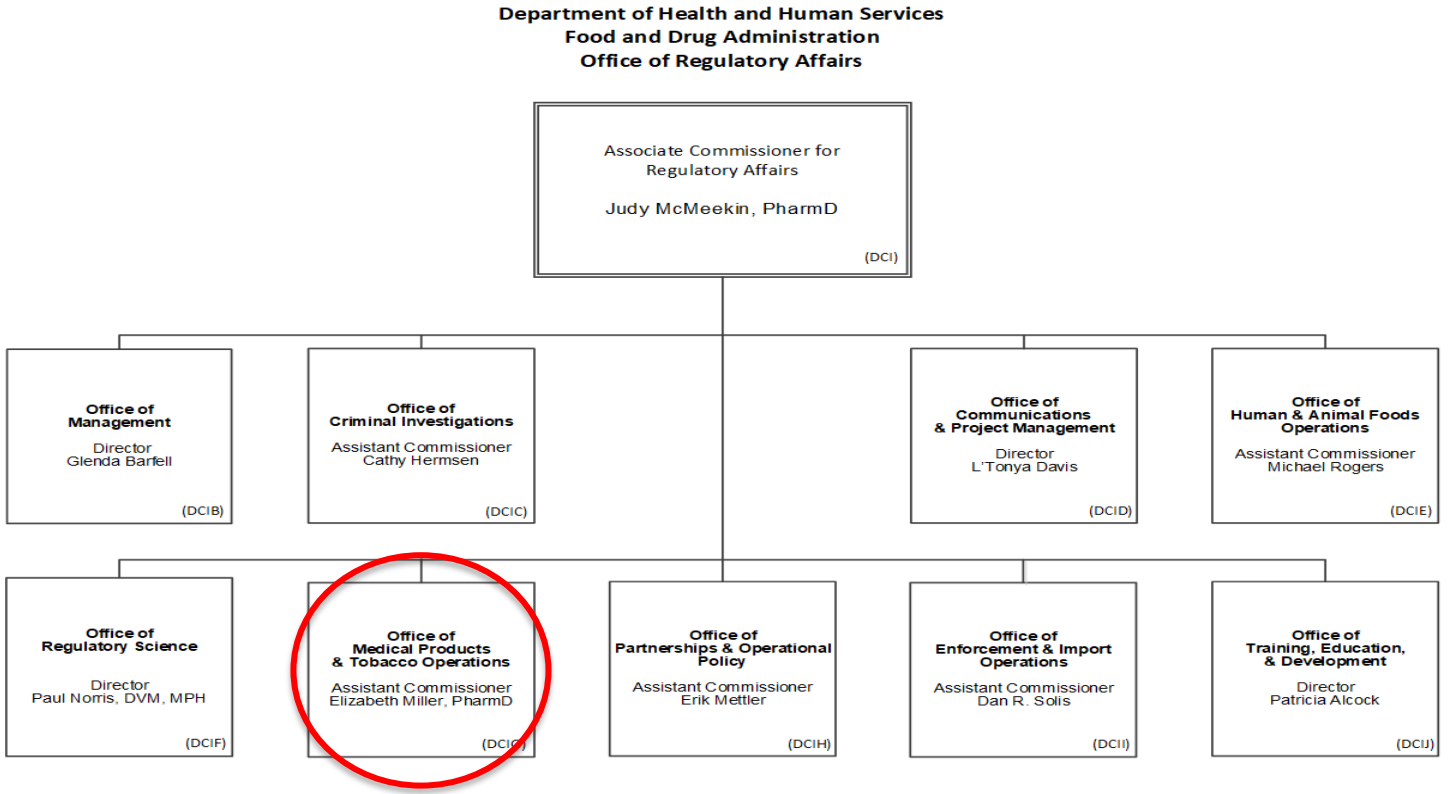
FDA Structural Organization



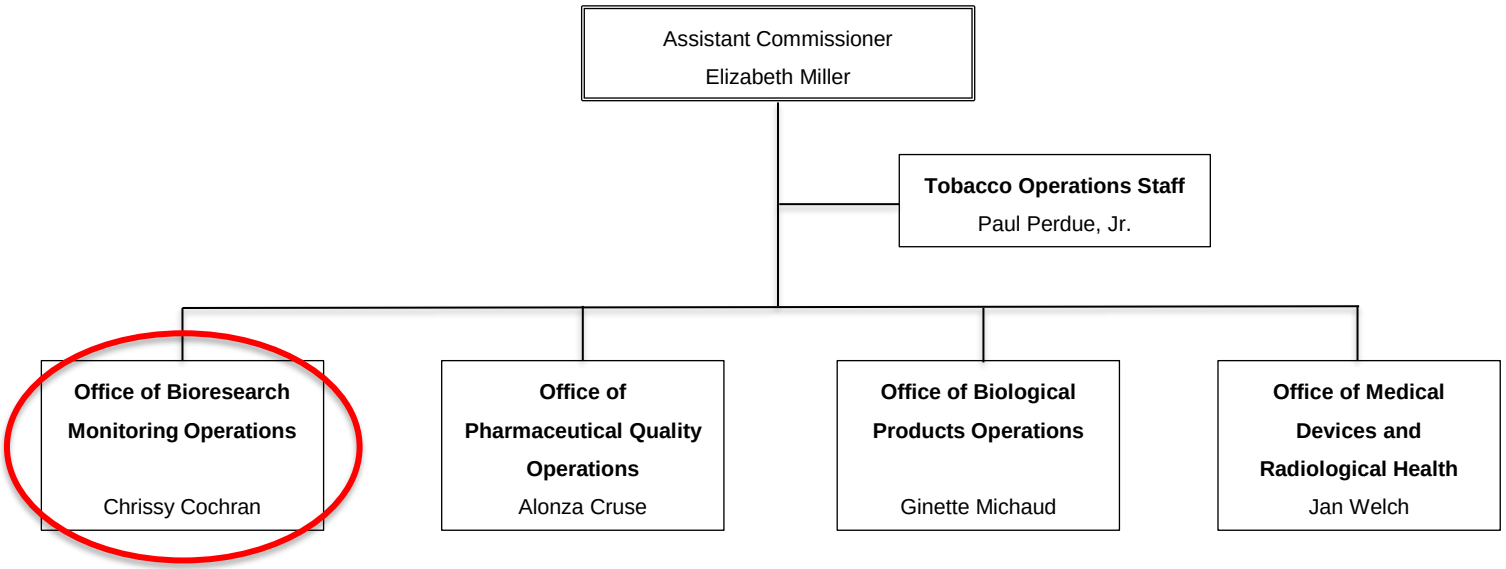
Center for Drug Evaluation & Research (CDER)



Office of Regulatory Affairs



Office of Medical Products and Tobacco Operations



Bioresearch Monitoring (BIMO) Program

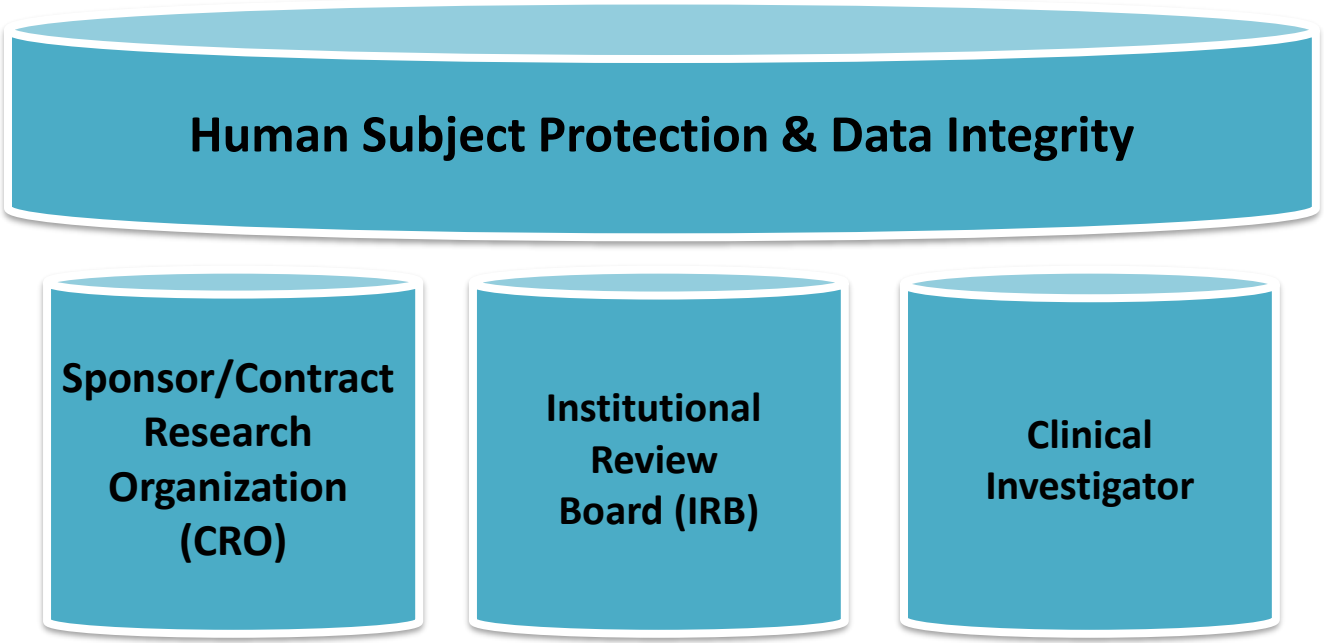
A comprehensive, FDA-wide program of on-site inspections and data audits, designed to monitor all aspects of the conduct and reporting of FDA-regulated research.

Objectives:

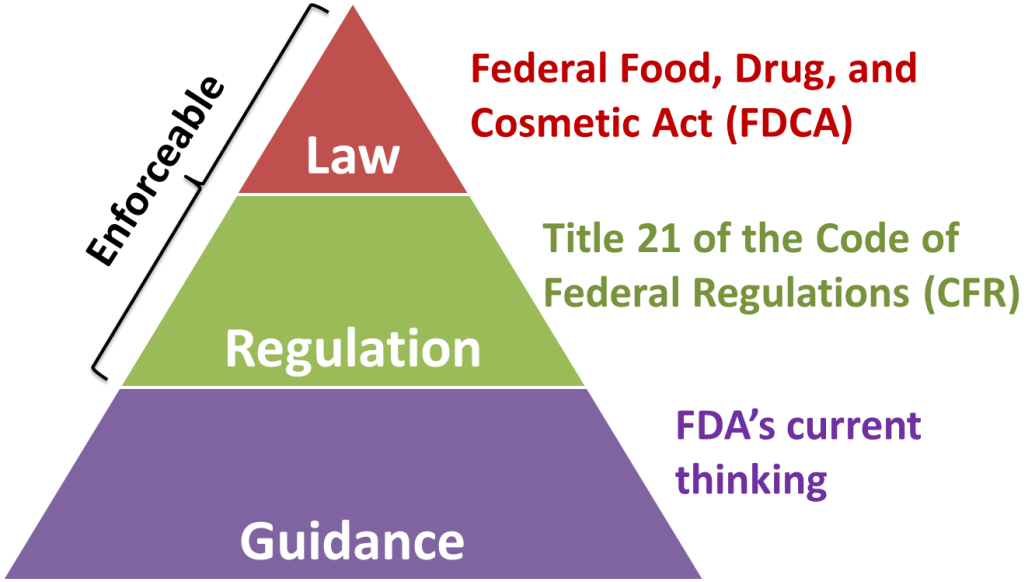
- Protect the rights, safety, and welfare of human research subjects
- Verify the accuracy, reliability, and integrity of clinical and non-clinical trial data submitted to FDA
- Assess compliance with FDA's regulations governing the conduct of clinical and non-clinical trials, including regulations for informed consent and ethical review

Bioresearch Monitoring

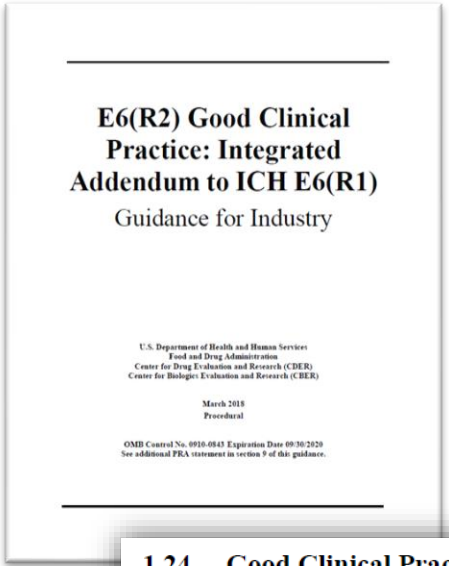
Good Clinical Practice



Governing Framework



Good Clinical Practice (GCP)



E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1)

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2018
Procedural

OMB Control No. 0910-0843 Expiration Date 09/30/2020
See additional PRA statement in section 9 of this guidance.

"A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected."

1.24 Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

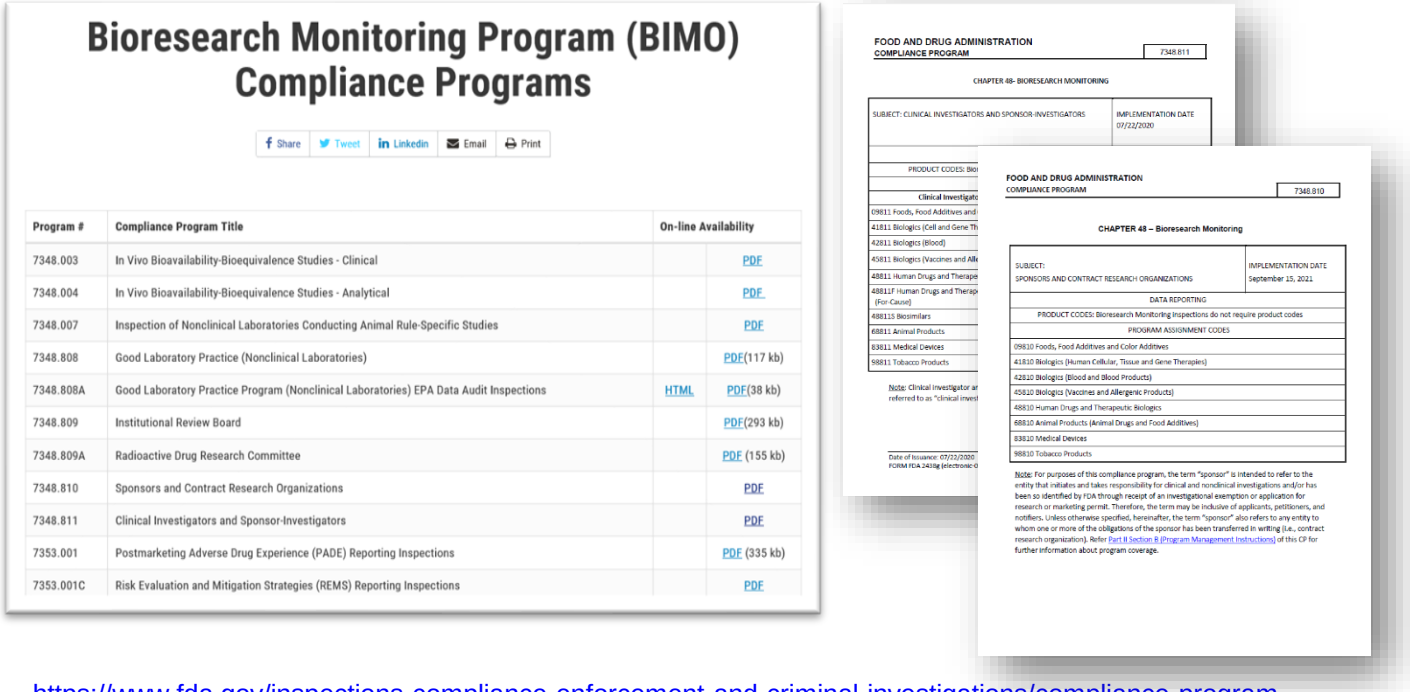
Regulations Relevant to GCP

- 21 CFR 11 – Electronic records and signatures
- 21 CFR 50 – Protection of human subjects
- 21 CFR 54 – Financial disclosure
- 21 CFR 56 – Institutional Review Boards
- 21 CFR 312 – Investigational new drug application
- 21 CFR 314 – Applications for FDA approval to market a new drug
- 21 CFR 320 - Bioequivalence

GCP Inspections under the BIMO Program

- Clinical Investigators (CI)
- Sponsors (Sp)
- Sponsor Investigators (SI)
- Contract Research Organizations (CRO)
- Institutional Review Boards (IRB)

Inspection Considerations: Compliance Programs



Bioresearch Monitoring Program (BIMO) Compliance Programs

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Program #	Compliance Program Title	On-line Availability	
7348.003	In Vivo Bioavailability-Bioequivalence Studies - Clinical		PDF
7348.004	In Vivo Bioavailability-Bioequivalence Studies - Analytical		PDF
7348.007	Inspection of Nonclinical Laboratories Conducting Animal Rule-Specific Studies		PDF
7348.808	Good Laboratory Practice (Nonclinical Laboratories)		PDF(117 kb)
7348.808A	Good Laboratory Practice Program (Nonclinical Laboratories) EPA Data Audit Inspections	HTML	PDF(38 kb)
7348.809	Institutional Review Board		PDF(293 kb)
7348.809A	Radioactive Drug Research Committee		PDF (155 kb)
7348.810	Sponsors and Contract Research Organizations		PDF
7348.811	Clinical Investigators and Sponsor-Investigators		PDF
7353.001	Postmarketing Adverse Drug Experience (PADE) Reporting Inspections		PDF (335 kb)
7353.001C	Risk Evaluation and Mitigation Strategies (REMS) Reporting Inspections		PDF

FOOD AND DRUG ADMINISTRATION
COMPLIANCE PROGRAM 7348.811

CHAPTER 48- BIORESEARCH MONITORING

SUBJECT: CLINICAL INVESTIGATORS AND SPONSOR-INVESTIGATORS | IMPLEMENTATION DATE 07/22/2020

FOOD AND DRUG ADMINISTRATION
COMPLIANCE PROGRAM 7348.810

CHAPTER 48 – Bioresearch Monitoring

SUBJECT: SPONSORS AND CONTRACT RESEARCH ORGANIZATIONS | IMPLEMENTATION DATE September 15, 2021

DATA REPORTING

PRODUCT CODES: Bioresearch Monitoring inspections do not require product codes

PROGRAM ASSIGNMENT CODES

09810 Foods, Food Additives and Color Additives
41810 Biologics (Human Cellular, Tissue and Gene Therapies)
42810 Biologics (Blood and Blood Products)
45810 Biologics (Vaccines and Allergenic Products)
48810 Human Drugs and Therapeutic Biologics
68810 Animal Products (Animal Drugs and Food Additives)
83810 Medical Devices
98810 Tobacco Products

Note: For purposes of this compliance program, the term "sponsor" is intended to refer to the entity that initiates and takes responsibility for clinical and nonclinical investigations and/or has been so identified by FDA through receipt of an investigational exemption or application for research or marketing permit. Therefore, the term may be inclusive of applicants, petitioners, and notifiers. Unless otherwise specified, hereinafter, the term "sponsor" also refers to any entity to whom one or more of the obligations of the sponsor has been transferred in writing (i.e., contract research organization). Refer Part II Section B (Program Management Instructions) of this CP for further information about program coverage.

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-program-manual/bioresearch-monitoring-program-bimo-compliance-programs

CDER BIMO* Inspections and Related Activities

- Prospective, real-time and retrospective oversight
- Multiple offices involved
  - CDER Office of New Drugs, Office of Surveillance and Epidemiology, Office of Clinical Pharmacology, and Office of Biostatistics: e.g. 30-day (Investigational New Drug application) safety reviews, protocol reviews, safety reports, marketing application reviews
  - CDER Office of Compliance (Office of Scientific Investigations): e.g. GCP inspection site selections (pre-market application review), complaint review, Institutional Review Board oversight
  - FDA Office of Regulatory Affairs: Inspections

*BIMO program also includes postmarketing safety programs: Postmarket Adverse Drug Experience (PADE) and Risk Evaluation and Mitigation Strategies (REMS)

Inspection Classifications

NAI

- **No Action Indicated**
- No violations identified

VAI

- **Voluntary Action Indicated**
- Violations identified, but do not meet threshold for OAI

OAI

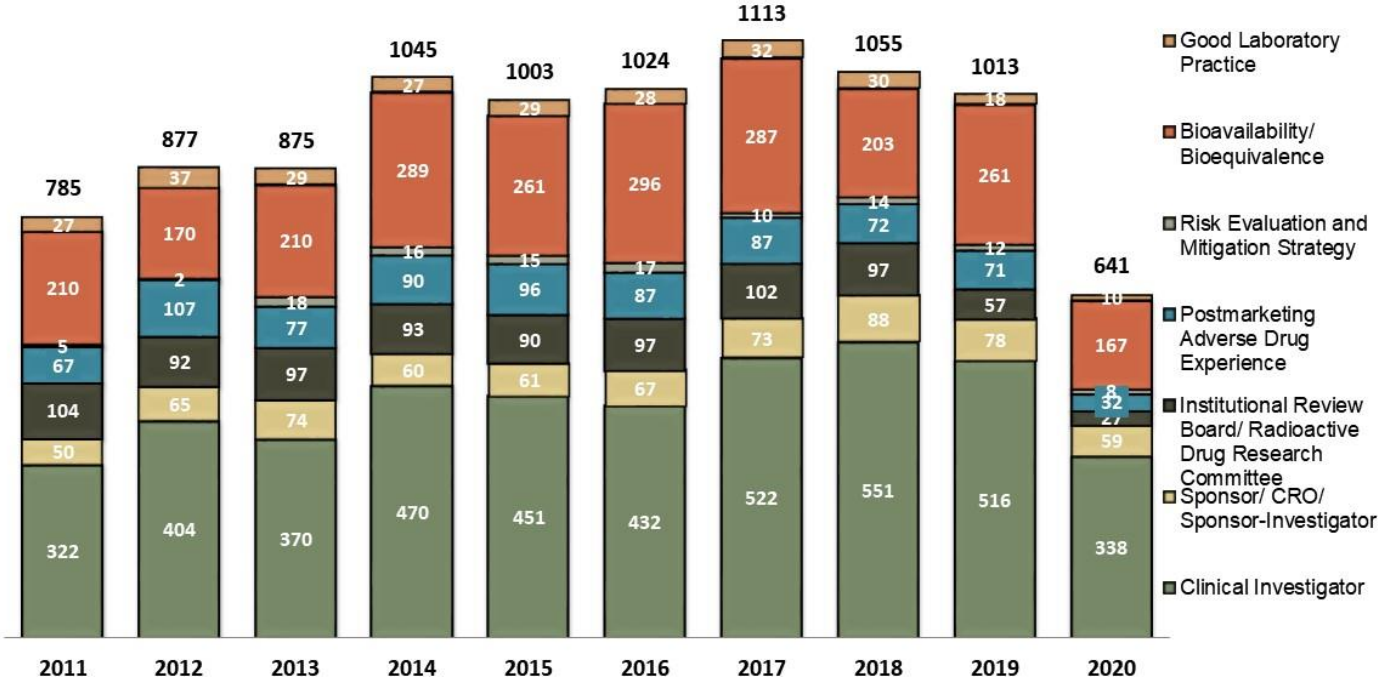
- **Official Action Indicated**
- Serious noncompliance
- Repeated or deliberate failure to comply with regulations

Remote Interactive Evaluations (RIE)

- RIE may be used to support regulatory decisions and oversight of establishments, while limiting unnecessary contact.
- FDA applies risk management methods and tools to determine when to request a facility's participation in a RIE.
- Resiliency Roadmap for FDA Inspectional Oversight: https://www.fda.gov/media/154293/download

CDER BIMO Inspection Activities*

(CDER, FY 2011 – FY2020)

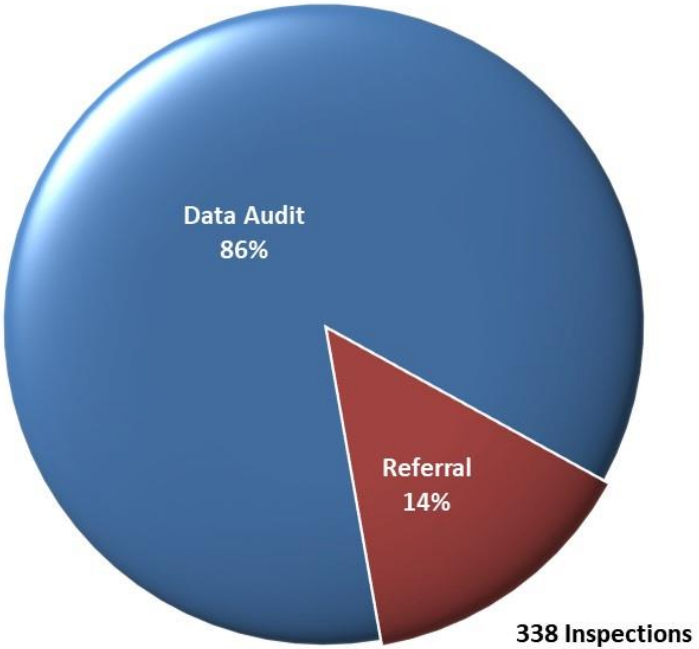


*Based on inspection start date – [Complis database as of Feb 9, 2021].

- Inspection numbers include use of alternative oversight tools (e.g. RIE).
- An inspection activity may involve multiple applications and/or studies.

Data Audit vs. Referral – CI*

(CDER, FY 2020)

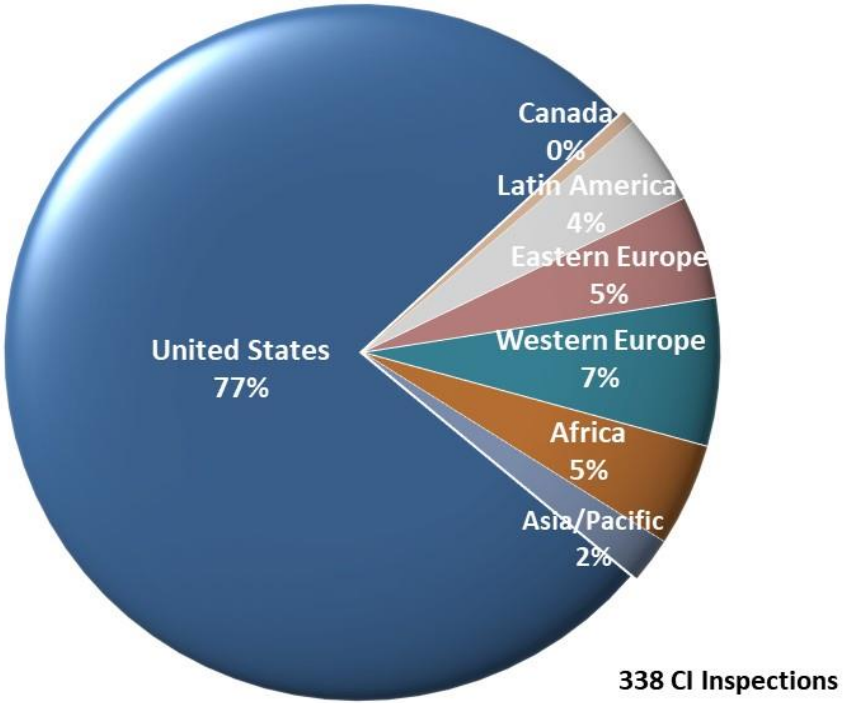


*Based on inspection start date – [Complis database as of Feb 9, 2021].

- Data Audits include Inspection Activity conducted in support of a marketing application.
- Referrals include Complaints, Required Reports, IRB/Sponsor Notifications, and other referrals-internal and external.

GCP Inspections by Location – CI*

(CDER, FY 2020)

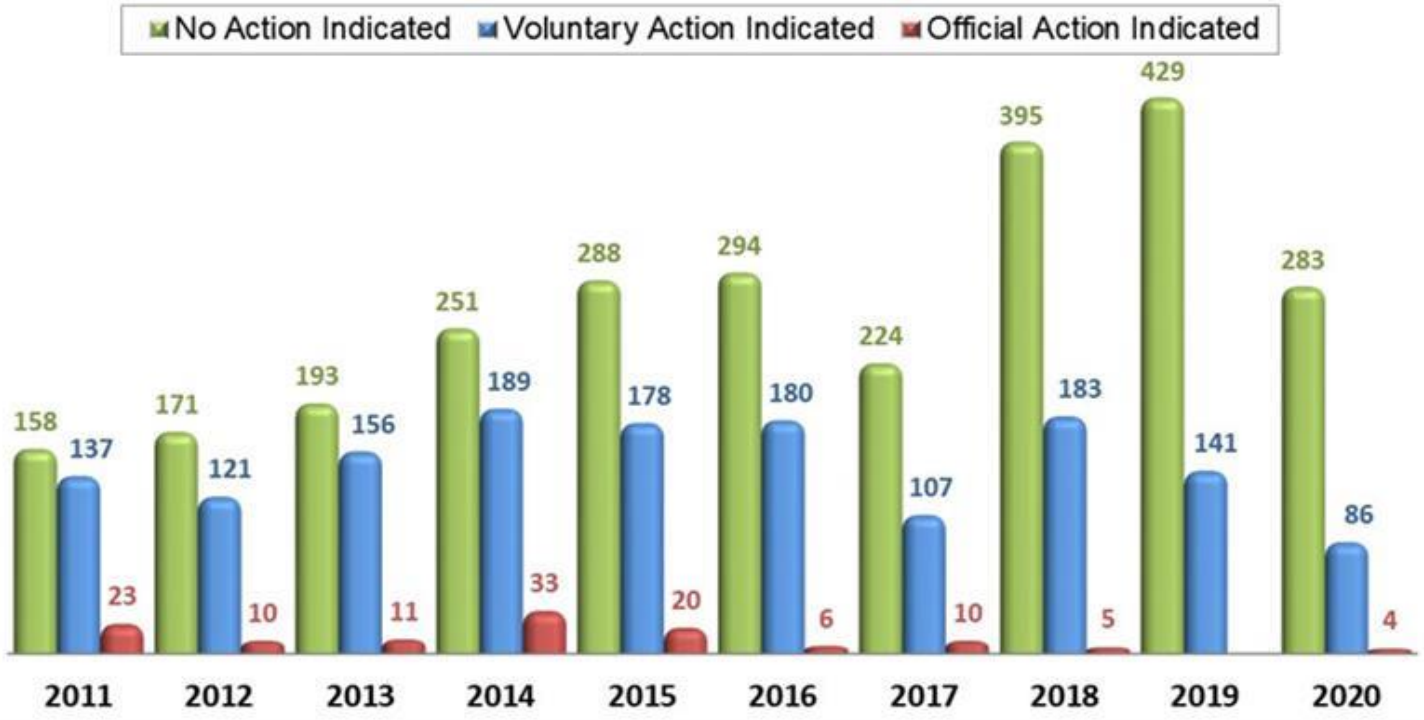


*Based on inspection start date – [Complis database as of Feb 9, 2021].

Final Classification – CI*

Domestic and Foreign

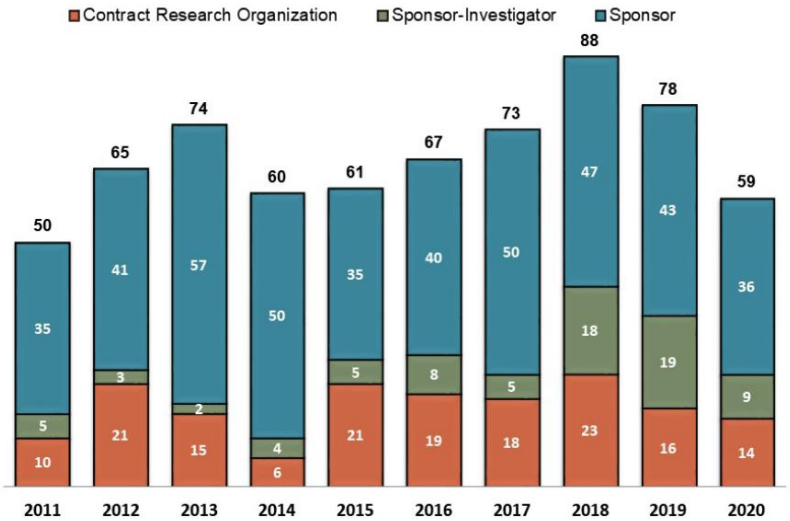
(CDER, FY 2011 – FY2020)



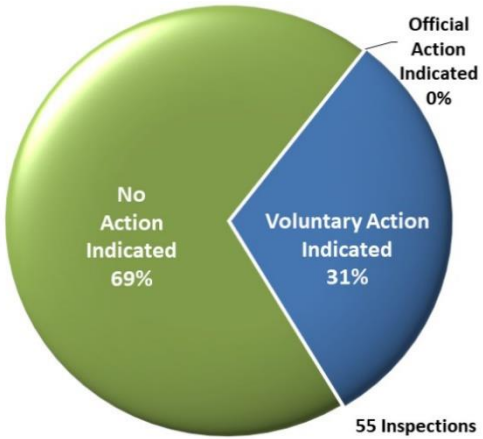
*Based on Letter Date and Final Classification [Complis database as of Feb 9, 2021].

GCP-Related Sponsor/CRO Inspections*

(CDER, FY 2011 – FY 2020)



*Based on inspection start date [Complis database as of Feb 9, 2021].



(CDER, FY 2020)

*Based on letter issue date [Complis database as of Feb 9, 2021]. Includes Sponsor-Investigator Inspection Activity.

Summary

- FDA's BIMO program monitors all aspects of clinical trial conduct.
- BIMO GCP inspections provide assurance of data integrity and human subject protection.
- BIMO GCP inspections ensure clinical trials are conducted according to applicable regulations.
- Multiple FDA/CDER offices are involved in clinical trial oversight.
- GCP Inspection activities include inspections for Clinical Investigators, Sponsors, Sponsor Investigators, CROs, IRBs.

Resources

BIMO Compliance Programs
https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-program-guidance-manual-cpgm/bioresearch-monitoring-program-bimo-compliance-programs

Code of Federal Regulations Title 21
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

FDA Guidance Documents
https://www.fda.gov/regulatory-information/search-fda-guidance-documents

FDA Investigations Operations Manual 2021
https://www.fda.gov/downloads/ICECI/Inspections/IOM/UCM607759.pdf

Remote Interactive Evaluations Guidance for Industry
https://www.fda.gov/media/147582/download

Challenge Question

Which of the following is NOT one of the BIMO program objectives?

A. Protect the rights, safety, and welfare of human research subjects.

B. Protect the public health by enforcing compliance with FDA's guidances governing the conduct of clinical and non-clinical trials.

C. Verify the accuracy, reliability, and integrity of clinical and non-clinical trial data submitted to FDA.

D. Assess compliance with FDA's regulations governing the conduct of clinical and non-clinical trials.

U.S. FOOD & DRUG ADMINISTRATION

Thank You!

Kelly M. K. Nolen, Ph.D.
Pharmacologist, Compliance Enforcement Branch
Division of Enforcement and Postmarketing Safety
Office of Scientific Investigations/Office of Compliance
CDER | US FDA

Kelly.Nolen@fda.hhs.gov