FDA's Use of Alternative Approaches to Evaluate GCP Compliance

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Clinical Investigator Training Course – December 12, 2024

Learning Objectives

- Describe changes in the clinical trial ecosystem impacting FDA's approach to evaluating GCP compliance.
- Discuss FDA's revised draft guidance on Remote Regulatory Assessments.
- Describe FDA collaborations with Foreign Regulatory Counterparts.
- Describe FDA's approaches to evaluating GCP compliance in clinical trials with innovative design elements.

Evaluating GCP Compliance: A History

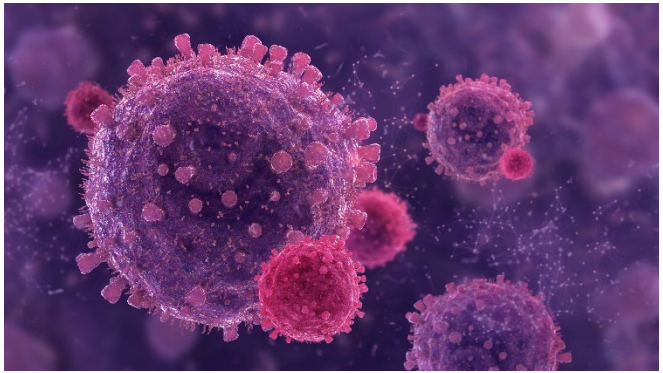
Inspections

Investigations

Information Sharing

Coverage of entire Compliance Program

Evaluating GCP Compliance: Changes



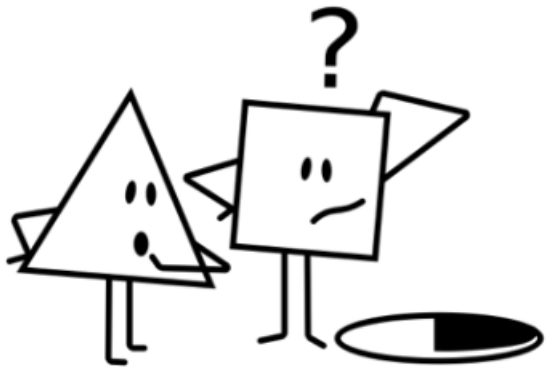
Remote Regulatory Assessments

Remote Regulatory Assessments

"An RRA is an examination of an FDA-regulated establishment and/or its records, conducted entirely remotely, to evaluate compliance with applicable FDA requirements. RRAs assist in protecting human and animal health, informing regulatory decisions, and verifying certain information submitted to the Agency."

Conducting Remote Regulatory Assessments Questions and Answers, Revised Draft Guidance (Jan. 2024)

RRAs are <u>not</u> . . .



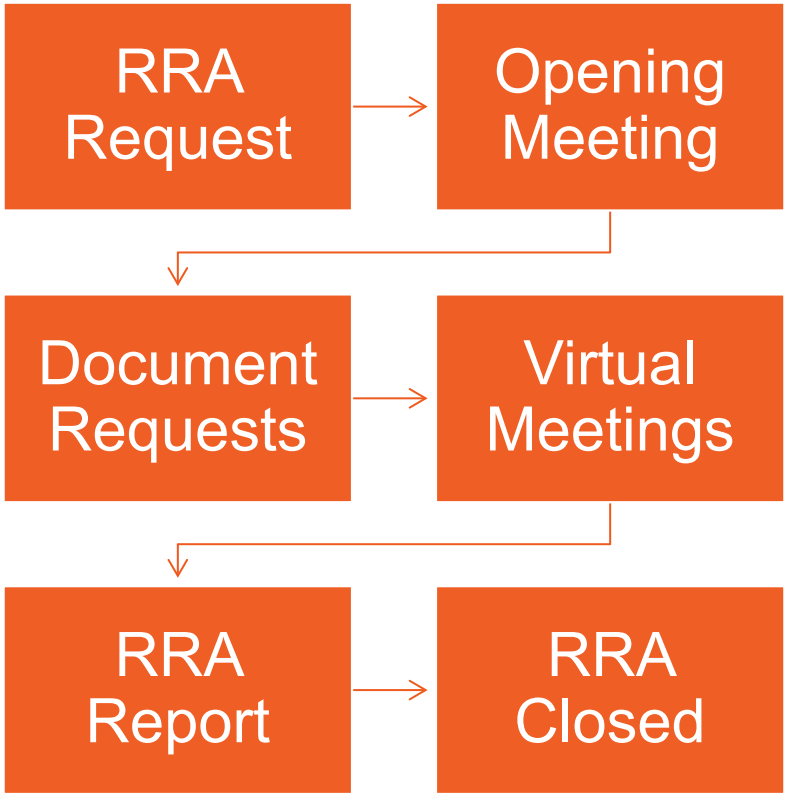
Created by R Diepenheim
from Noun Project

- Inspections
- Something you can ask for
- Intended to limit or replace other ways FDA gets information

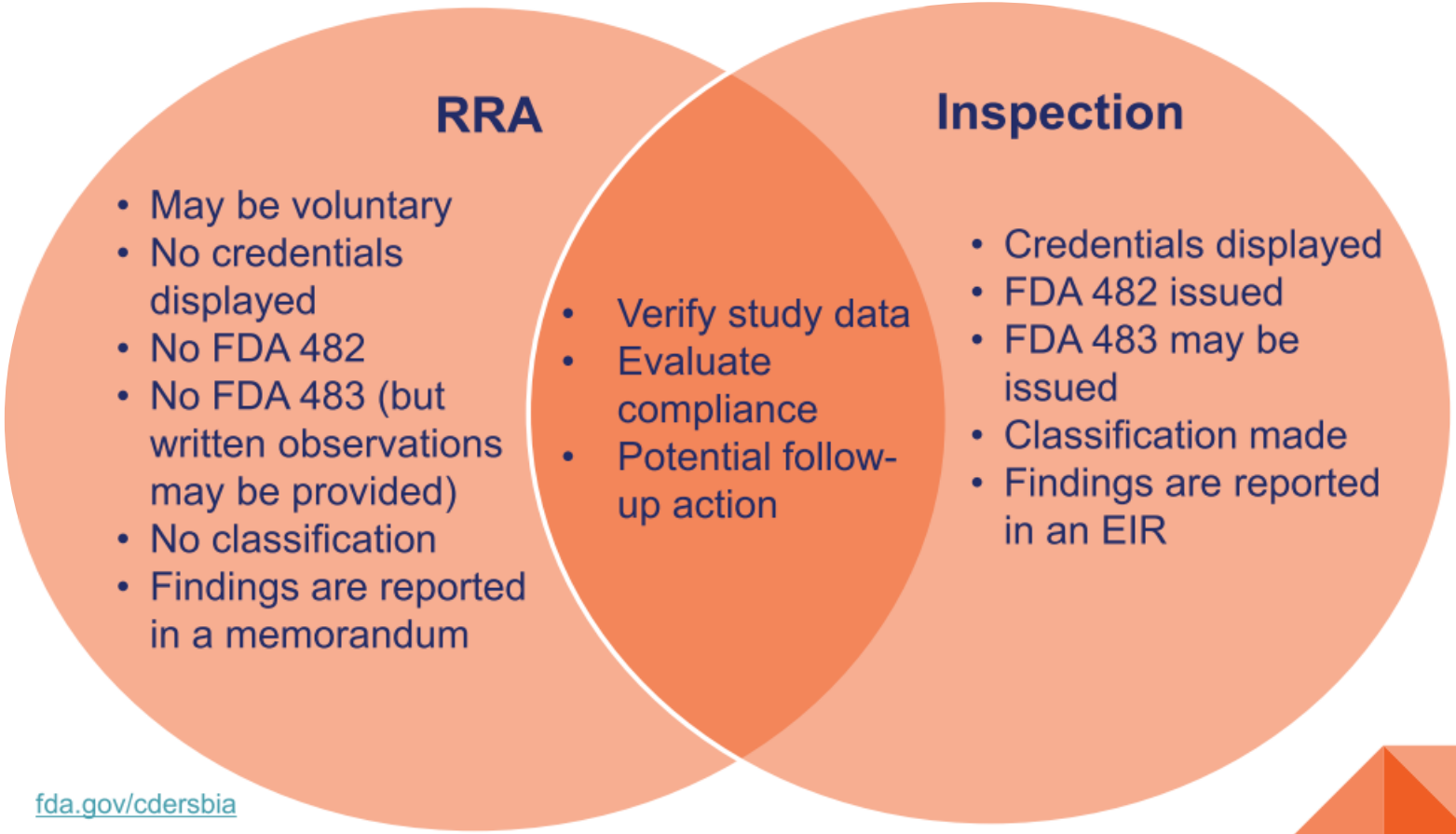
Types of RRAs

- RRA describes a category of activities.
- RRAs may be mandatory or voluntary.
  - Mandatory RRAs are conducted under legal authority mandating participation.
  - Voluntary RRAs are not conducted under legal authority. FDA requests participation.
  - CDER clinical investigator RRAs typically are voluntary.

RRA Process


RRA Request
Opening Meeting
Document Requests
Virtual Meetings
RRA Report
RRA Closed

Comparing RRAs and Inspections



How to Prepare for an RRA

1. Commit
2. Clarify
3. Organize
4. Staff
5. Connect

Challenge Question #1

Which of the following is <u>true</u> for remote regulatory assessments:

A. Always mandatory.

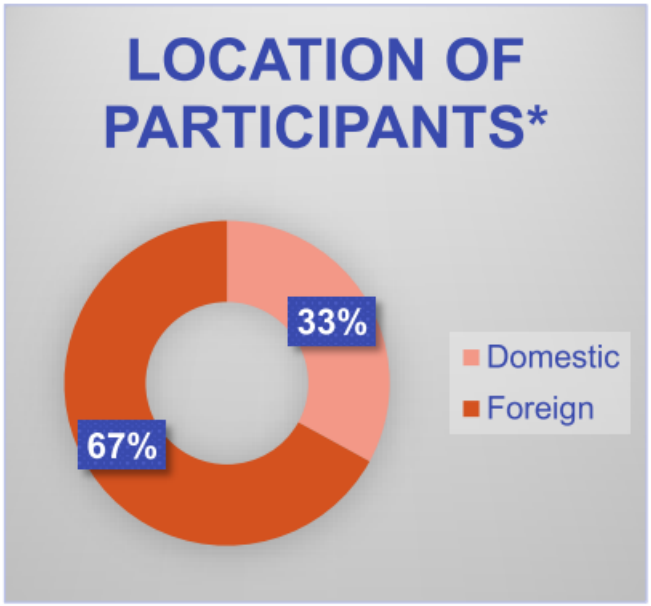
B. Begin with FDA presenting credentials and issuing an FDA 482.

C. May involve interactive elements, such as screen sharing.

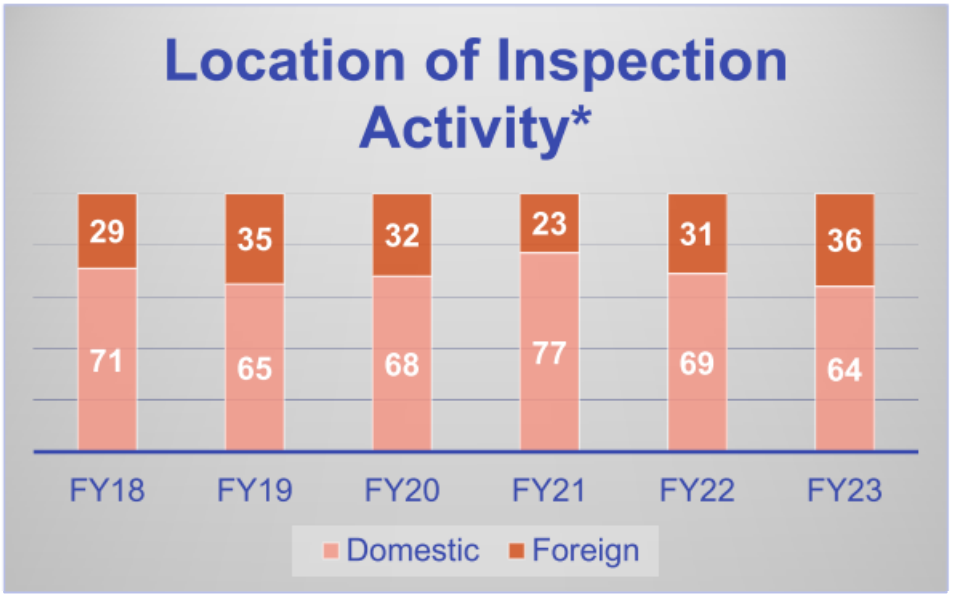
D. May result in issuance of an FDA 483.

Collaboration with Foreign Regulatory Counterparts

Foreign Clinical Trials

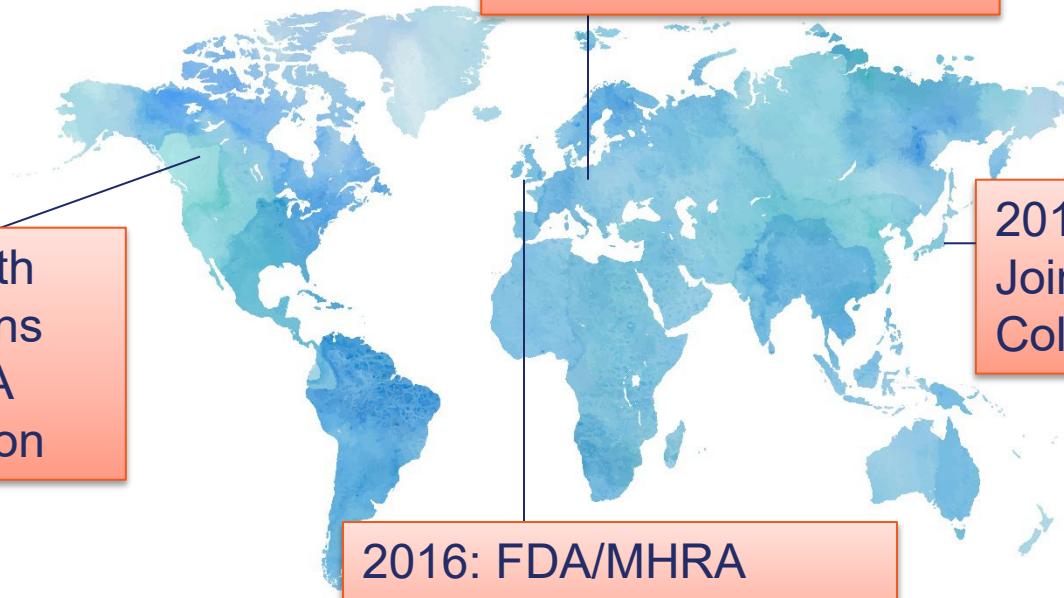


*In clinical trials supporting 54 novel approvals in CY 2023. Based on 2023 Drug Trials Snapshots Summary Report.



*Inspection activities in support of marketing applications issued by CDER/OSI. Based on Inspection Activity start data as a percentage. Data from FDA's Compliance Program Information System (Complis) database.

International Collaboration



2009: FDA/EMA Collaboration

2020: Health Canada joins FDA/MHRA Collaboration

2017: PDMA Joins FDA/EMA Collaboration

2016: FDA/MHRA Collaboration

International Collaboration

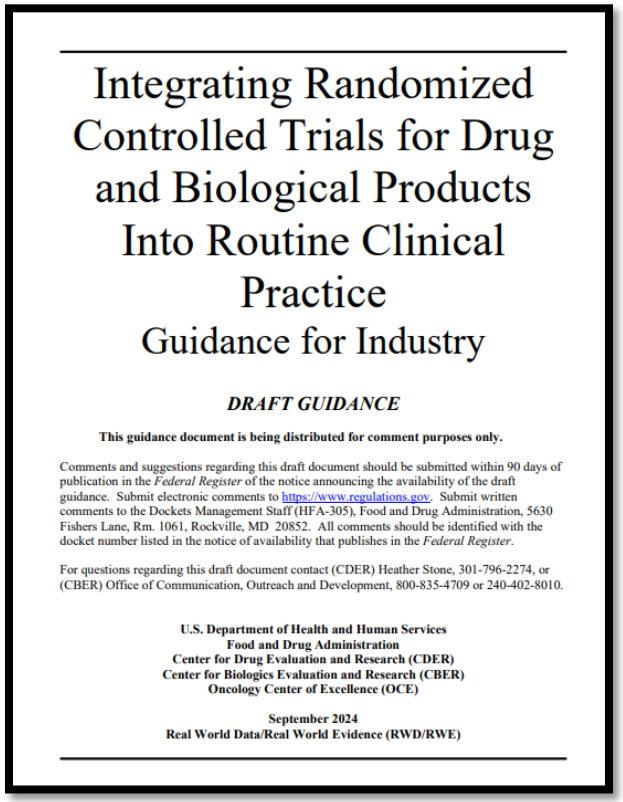
Share:

- inspection information (planning, outcomes)
- information about GCP-related legislation, guidance, and policy

Conduct collaborative inspections (observational and joint)

Evaluation of GCP in Innovative Clinical Trials

Innovating Approaches to Evaluation



Integrating Randomized Controlled Trials for Drug and Biological Products Into Routine Clinical Practice

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER) Heather Stone, 301-796-2274, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

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)
Oncology Center of Excellence (OCE)

September 2024
Real World Data/Real World Evidence (RWD/RWE)

"... bioresearch monitoring inspections by FDA assess practices and procedures likely to have a meaningful impact on the reliability of the results and on the rights, safety, and well-being of participants. Inspections also assess whether important protocol deviations occurred during a trial (e.g., failing to obtain informed consent, randomizing patients who did not meet enrollment criteria, failing to report important safety events) and any systemic or serious issues that occurred during the conduct of the trial."

Real-World Data & Real-World Evidence

Real-World Data

Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources

- EHR Data
- Claims Data
- Registry Data
- DHT Data

Real-World Evidence

Clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD

Evaluating Trials Incorporating Real-World Evidence

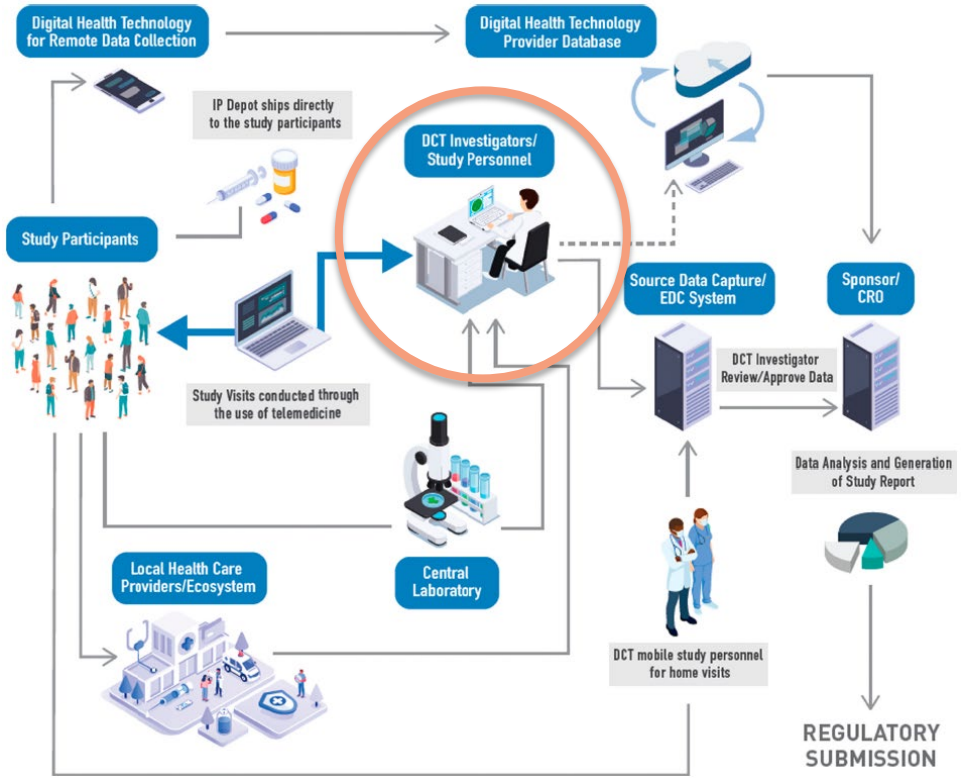
- Source Data Verification
- Data Quality Assessment
- Data Curation, Transformation, and Analysis Assessment

Evaluating Trials Incorporating DHTs

- FDA does not intend to inspect individual DHTs for source data IF:
- Data captured by the DHT (including all metadata) ARE:
  - securely transferred to and retained in the durable electronic data repository
  - according to the sponsor's pre-specified plan
- FDA considers electronic data located in the first durable database to which the data are transferred to be source data

FDA Guidance, Digital Health Technologies for Remote Data Acquisition in Clinical Investigations (Dec. 2023)

Evaluating Trials Incorporating Decentralized Elements



"For FDA inspections of clinical investigators, the investigator should identify a physical location where a responsible person is available to facilitate the FDA inspectors' access to trial-related records (either paper or electronic access) for participants under the clinical investigator's care and to facilitate interviews with trial personnel (either in person or remotely)."

FDA Guidance, Conducting Clinical Trials with Decentralized Elements (Sept. 2024)

fda.gov/cdersbia

Khin NA et al. Tackling Challenging Data Integrity Topics in 2020: Update on Good Clinical Practice Perspectives from the US FDA and MHRA UK. Clin Pharmacol Ther 112, 31-43 (2022)

Challenge Question #2

Which of the following is <u>not</u> real-world data?

A. Data collected in electronic health records during routine clinical care.

B. Data collected by a study nurse during a study visit at the investigator's site.

C. Data from insurance claims for healthcare provider services.

D. Data from a disease-specific registry.

Evaluating GCP Compliance: A Future

Range of well-defined, fit for purpose oversight options that can be deployed as appropriate

Flexible, efficient oversight that maximizes resources and robustly supports regulatory decision-making


FDA
U.S. FOOD & DRUG
ADMINISTRATION