U.S. FOOD & DRUG ADMINISTRATION

International Clinical Trials: GCP Perspective

Kassa Ayalew, M.D., M.P.H.
Division of Clinical Compliance Evaluation
Office of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research

Disclaimer

The views expressed in this presentation are those of the speaker and not necessarily those of the Food and Drug Administration

Objectives

To share information about international clinical trials from GCP perspective

To provide you information on how to comply with FDA's regulatory requirements for international clinical trials

International Clinical Trials

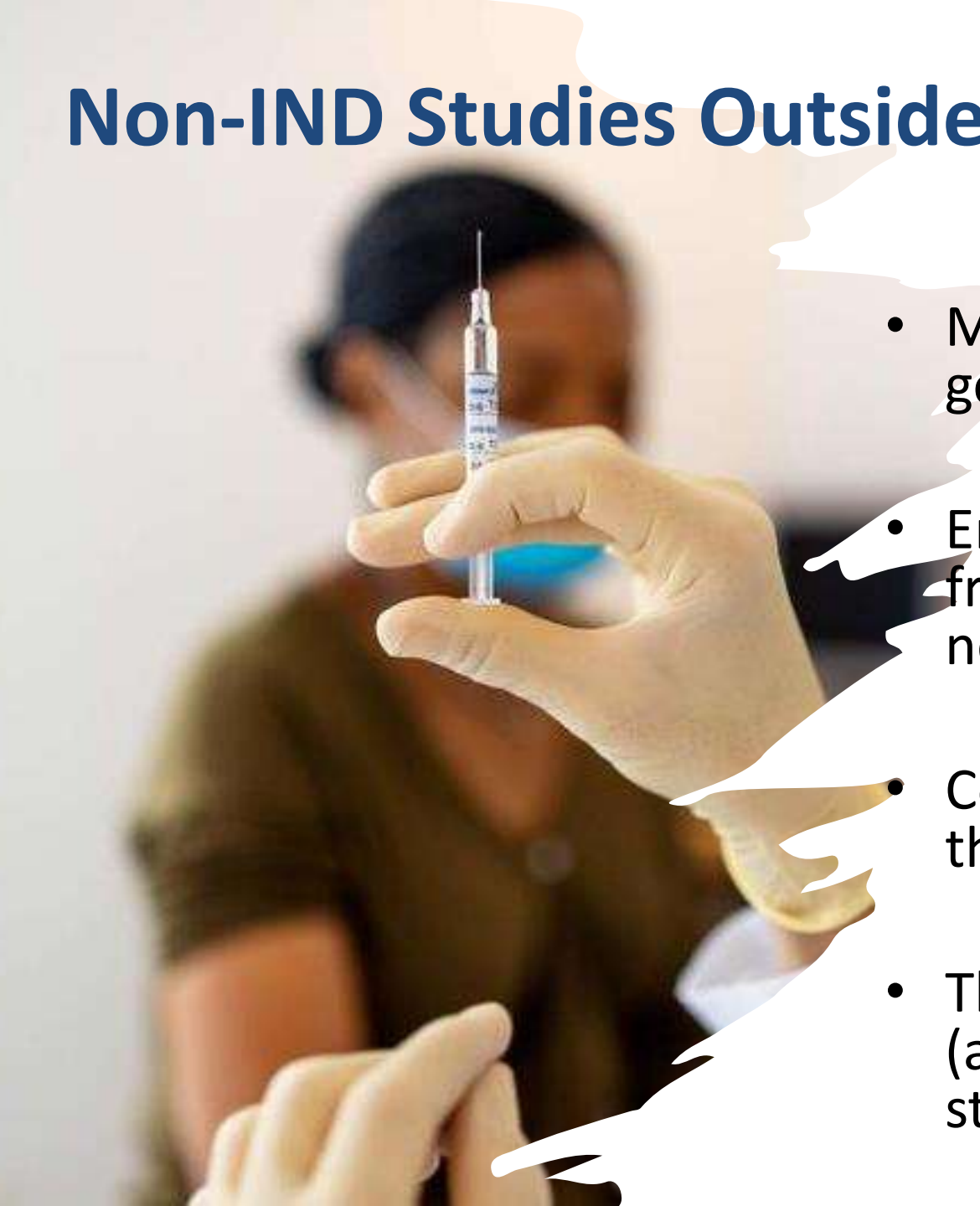
- Clinical trails are increasingly global
- They are conducted under a variety of scenarios
- Some trials are based solely on foreign clinical data

Conducting Clinical Trials Outside United States

- Investigational New Drug (IND) is not required
- If a clinical trial is conducted under an IND, IND requirements must be met unless waived
- If a clinical trial is not conducted under IND, one must ensure that the trial complies with the requirements in 21 CFR 312.120

An IND is a request for FDA authorization to ship an investigational drug across state lines for use in human clinical trials.

Non-IND Studies Outside the United States



- Must conduct the study in accordance with good clinical practice (GCP)
- Ensuring that FDA is able to validate the data from the study through an onsite inspection, if necessary
- Conducting studies in a manner comparable to that required for IND studies
- The GCP requirements encompass both ethical (approval by IEC/IC) and data integrity standards for clinical studies.

How are Clinical Trials Conducted in the United States

- In the United states investigators are required to submit an IND to FDA if they intend to conduct a clinical investigation unless studies meet specific regulatory exemption criteria.

- When a clinical study is conducted under an IND, all FDA IND requirements (21CFR 312) must be met unless waived.

Investigator Responsibilities for IND Studies

1) Ensuring that an investigation is conducted according to the signed investigator statement, the investigational plan, and applicable regulations. 312.60

2) Ensuring control of drugs under investigation; including storage of the investigational drug . 312.61

3) Maintaining adequate records of the disposition of the drug, accurate case histories. 312.62

4) Providing investigator reports: progress reports, safety reports, final. 312.64

5) Ensuring IRB review, approval and reporting requirements. 312.66

6) Ensuring FDA has access to inspect investigator's records and reports. 312.68

7) Ensuring that informed consent is adequately obtained.312.60

8) Providing financial disclosure to sponsor. 312.64

The investigator responsibilities are covered under Part 312.60 to 312.70 Investigational New Drug Application Regulations

Exemptions from IND Requirements

Exemption from IND will be granted if **all of** the following requirements are met:

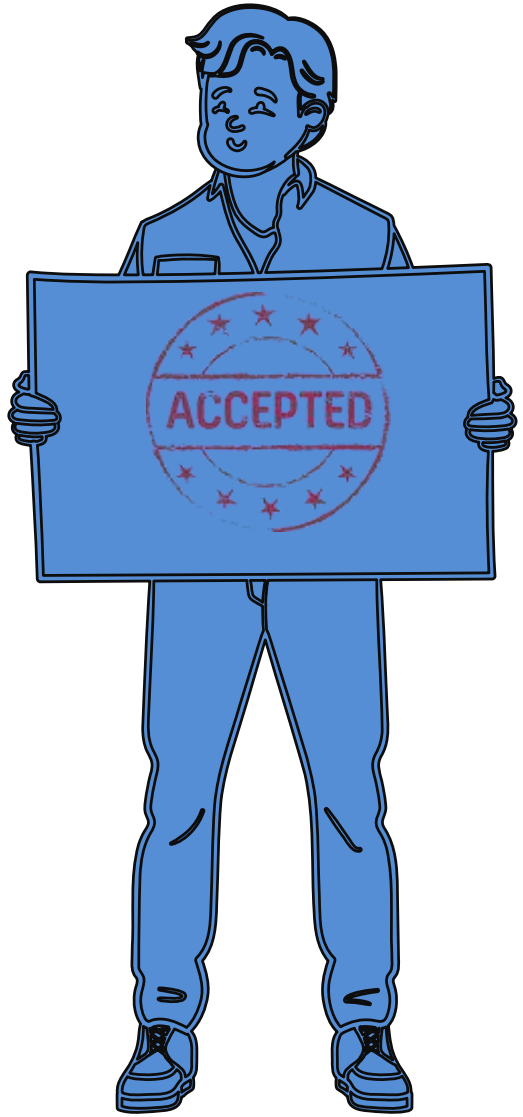
The drug product for the planned investigation is **lawfully marketed** in the U.S.	The planned investigation is **not intended to support new indication**/or significant change in labeling	The planned investigation does not involve a route of administration or dosage level or use in a patient population or other factor that **significantly increases risk**	The investigation is conducted in compliance with part 56 (**Institutional Review Board**) and part 50 (**Informed Consent**) regulations	The investigation is conducted in compliance with 21 CFR 312.7 (**promotion and commercial distribution** of an investigational new drug) regulations

Acceptance of Foreign Data from Non-IND Trials

Foreign data should be:

1. Applicable to the **U.S. population** and medical practice
2. Generated by **investigators** of recognized competence
3. Considered **valid** without an inspection
4. Validated through **inspection** when it deems necessary

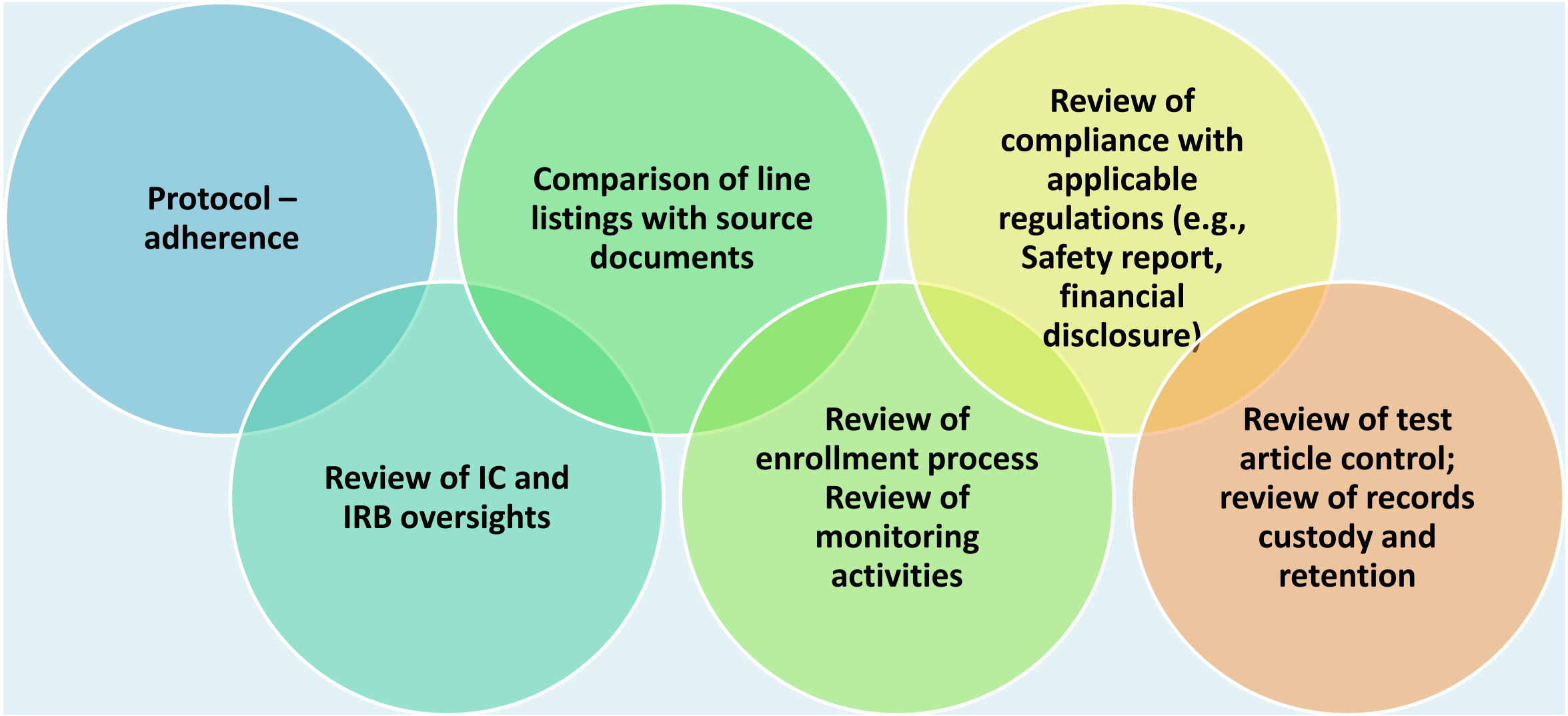
[21 CFR 314.106.(b)]



Inspection of Clinical Investigator

- Knowledge of Clinical Investigator regulations and important guidances
- Understanding of Clinical Investigator responsibilities and complying with regulatory expectations
- Adherence to Code of Federal Regulations

Inspection Areas of Focus



Sponsor / CRO Inspection Focus

Organization and Personnel

Registration of Trials

Selection and Communication with Investigators

Monitors and Monitoring

Quality Assurance (Auditing)

Adverse Event Reporting

Data Handling/Data Audit

Control of Investigational Product(s)

Review of Automated (Computerized) Processes

Electronic Records and Electronic Signatures

Recordkeeping and Record Retention

Financial Disclosure

Take Home Point

Wherever clinical trials are conducted, it is important to have drug development programs that reliably produce high quality data acquired in a manner that will not jeopardize the rights, safety, or welfare of trial participants

FDA's Principal Deputy Commissioner, Janet Woodcock, M.D.


FDA
U.S. FOOD & DRUG
ADMINISTRATION