International Clinical Trials: GCP Perspective

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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

Introduction to International Clinical Trials

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

Relevant FDA Regulations

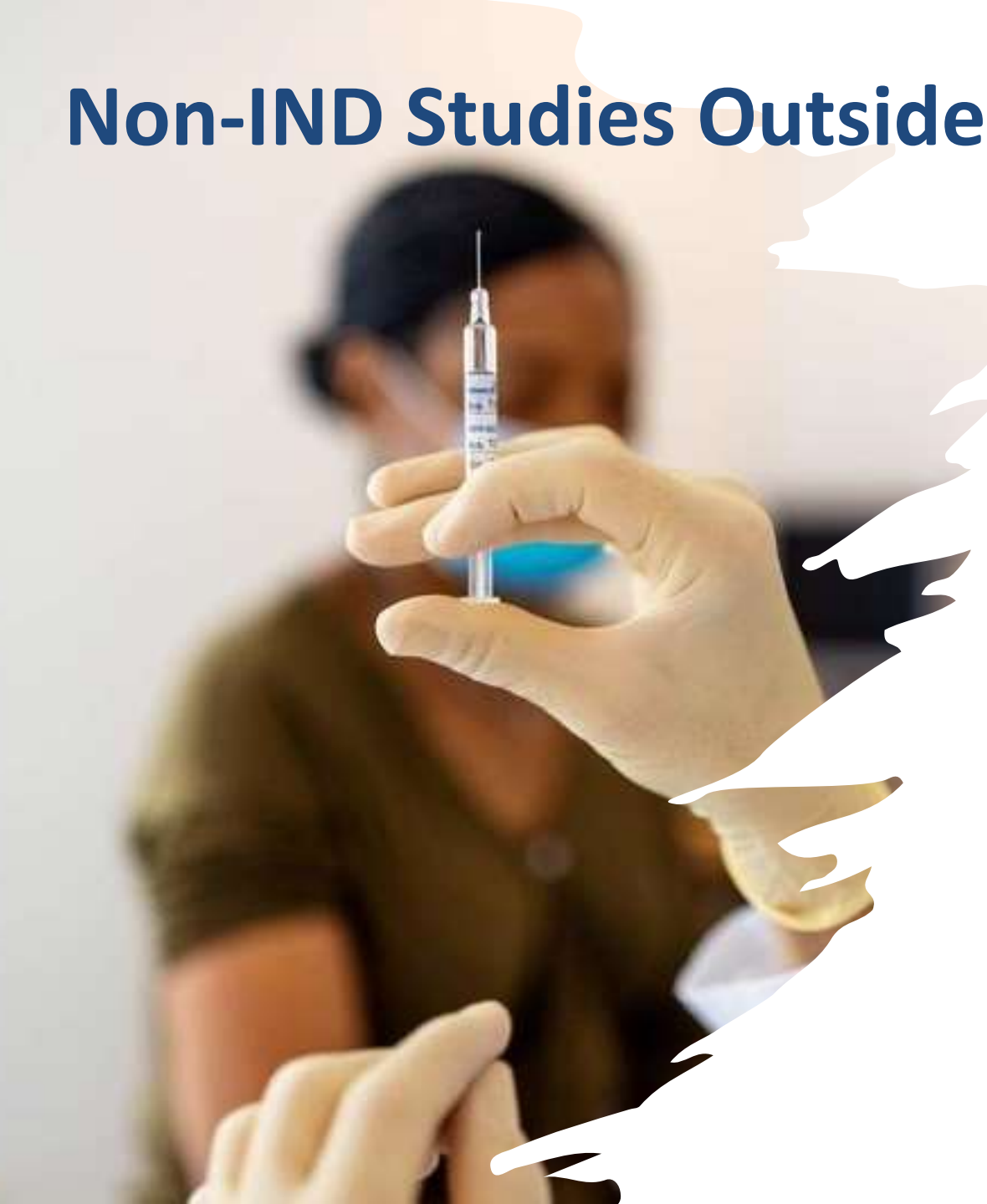
- 21 C.F.R. Part 312: Investigational New Drug (IND) Application
- 21 C.F.R. Part 312.120 : Foreign clinical studies not conducted under an IND
- 21 C.F.R. Part 314 - Applications for FDA approval to market a new drug
- 21 C.F.R. Part 50: Protection of Human Subjects
- 21 C.F.R. Part 54: Financial Disclosure by Clinical Investigators
- 21 C.F.R. Part 56: Institutional Review Boards
- 21 C.F.R. Part 11: Electronic Records, Electronic Signatures

Conducting Clinical Trials Outside United States

- 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, the sponsor must ensure that the trial complies with the requirements in 21 CFR 312.120

An IND is a request for FDA authorization to administer an investigational drug to humans.

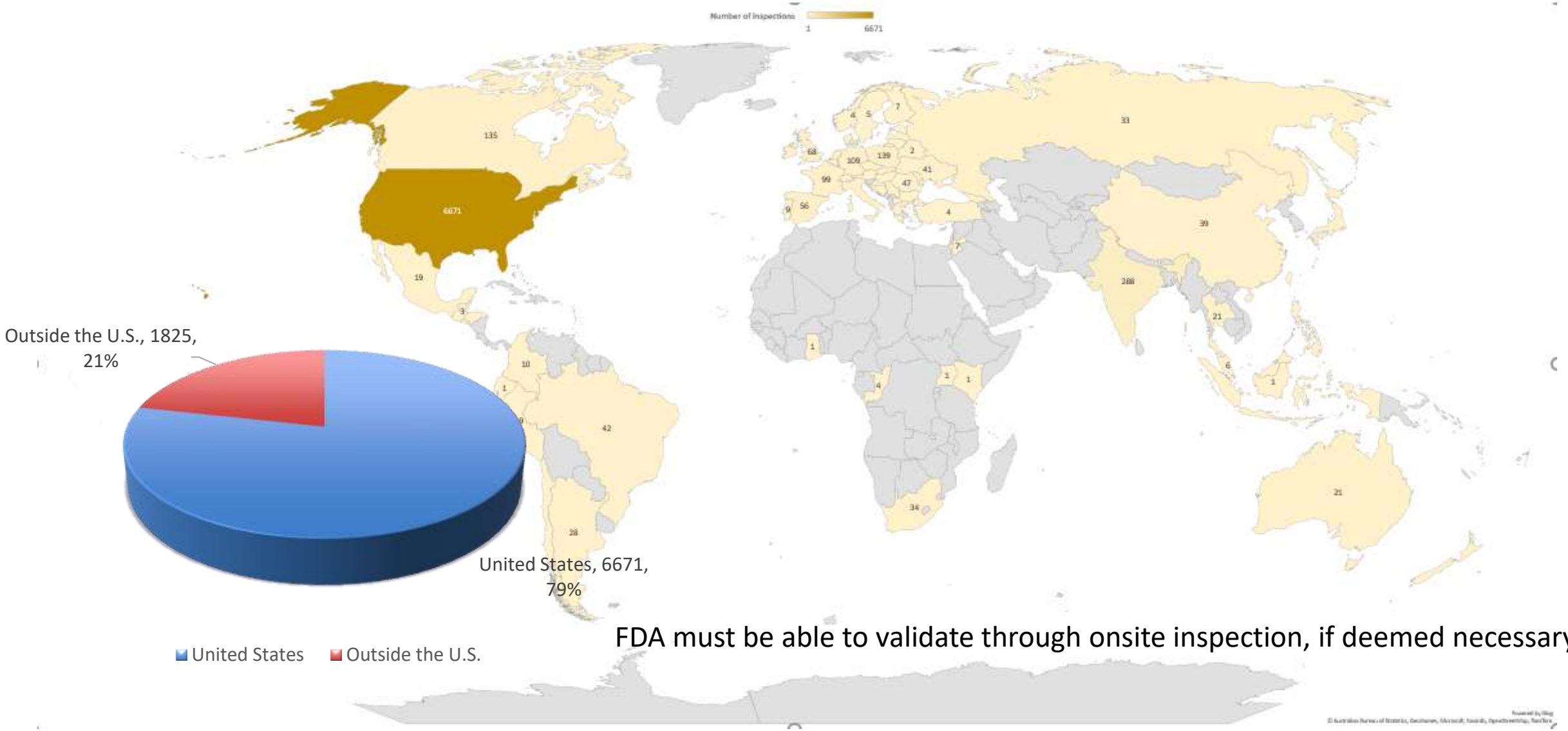
Non-IND Studies Outside the United States



1. Must conduct the study in accordance with good clinical practice (GCP)

2. FDA should be able to validate the data from the study through an onsite inspection, if necessary

Foreign and Domestic Inspections, FY 2012-2022



FDA must be able to validate through onsite inspection, if deemed necessary

Clinical Trial Requirements 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 (FDA Form 1572), the **investigational plan, and applicable regulations**
2. Ensuring **control of drugs** under investigation; including **storage** of the investigational drug
3. Maintaining **adequate records** of the disposition of the drug**, accurate case histories**
4. Ensuring record **keeping and retention**
5. Providing **investigator reports**: progress reports, safety reports, final
6. Ensuring **IRB review**, approval and reporting requirements
7. Ensuring **FDA has access** to inspect investigator's records and reports.
8. Ensuring the **protection of the rights, safety, and welfare** of subjects
9. Ensuring that **informed consent** is adequately obtained
10. Providing **financial disclosure** to sponsor

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:

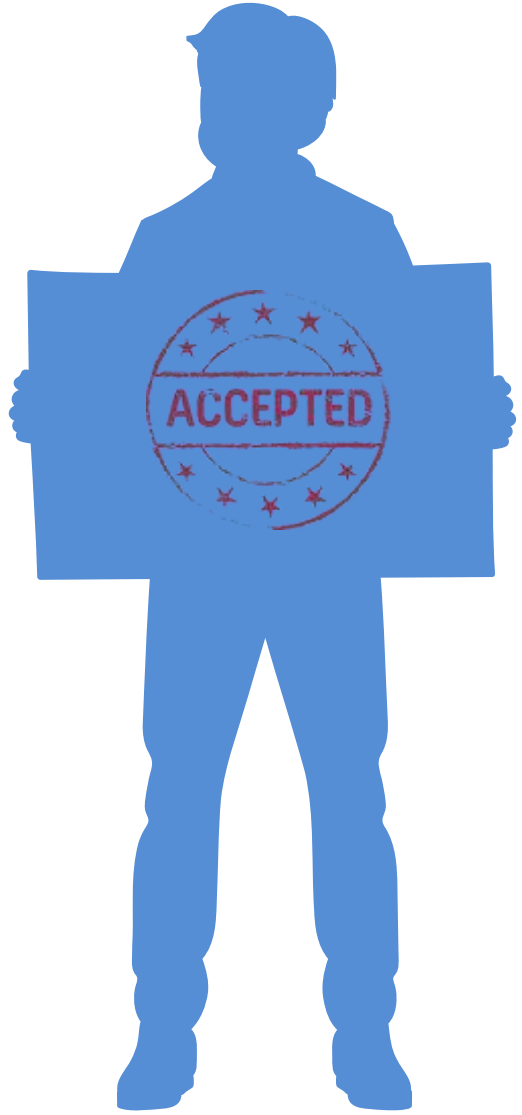
1. The drug product for the planned investigation is lawfully marketed in the U.S.
2. The planned investigation is not intended to support new indication/or significant change in labeling
3. The planned investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases risk
4. The investigation is conducted in compliance with part 56 (Institutional Review Board) and part 50 (Informed Consent) regulations
5. 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)]



General Expectations During Inspection of Clinical Investigators

FDA regularly performs inspections of clinical investigators/ sites to ensure compliance with GCP and FDA's regulatory requirments

FDA investigators may inspect study binders, drug accountability records, consents, medical records, tests and procedures, case report forms, qualifications of investigator and study staff, and all other documents that relate to a study

Inspection Areas of Focus

1) Protocol – adherence

2) Review of IC and IRB oversights

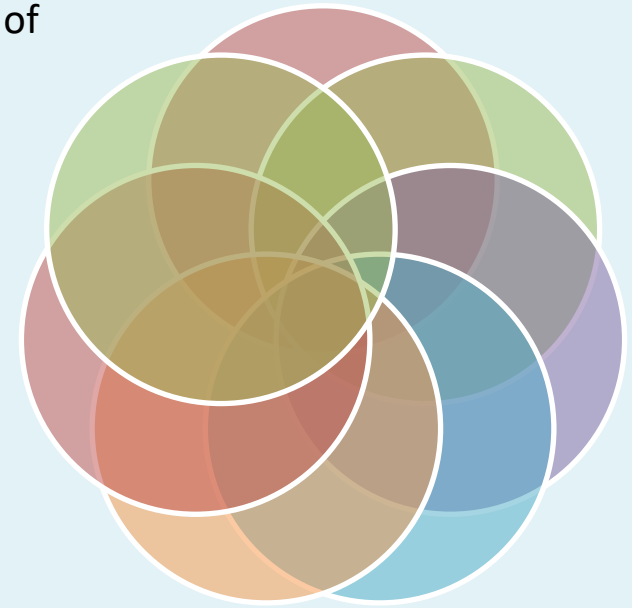
3) Comparison of line listings with source documents and verification of reported data and quality

4) Review of enrollment process
Review of monitoring activities

5) Review of reporting to sponsor

6) Review of compliance with applicable regulations (e.g., Safety report, financial disclosure and updates)

7) Review of test article control; review of records custody and retention



Take Home Point

It is important to know FDA's regulatory requirements for international clinical trials are critical to reliably produce high quality data and not to jeopardize the rights, safety, or welfare of trial participants