Bioavailability/Bioequivalence Site Evaluation During the Pandemic

Makini K. Cobourne-Duval, Ph.D.
Pharmacologist
Office of Study Integrity and Surveillance (OSIS)
Office of Translational Sciences
Center for Drug Evaluation and Research (CDER) | US FDA

Generic Drugs Forum 2021: Lifecycle of a Generic Drug – April 28-29, 2021

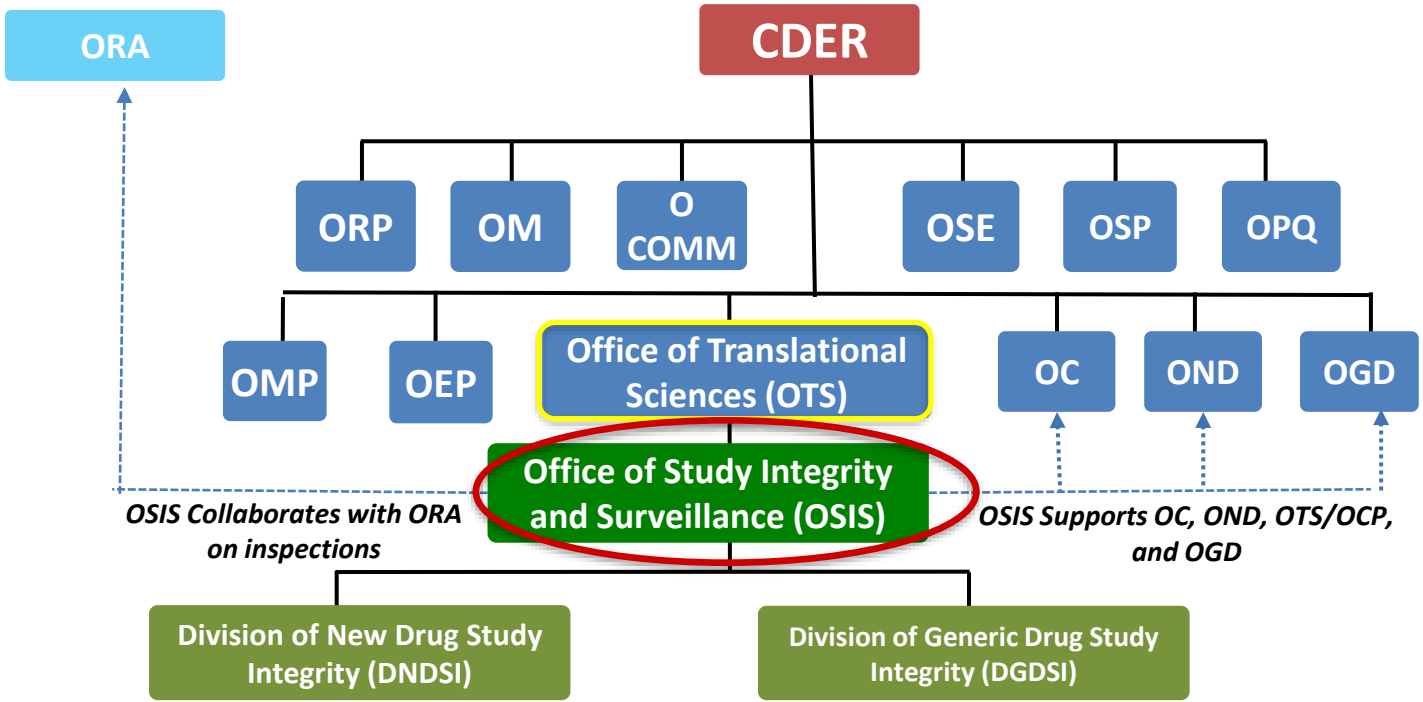
Learning Objectives

- Describe the role of OSIS in the Drug Life Cycle
- Explain how OSIS has adopted new techniques to accomplish the Agency's mission in the face of the COVID-19 pandemic

Outline

- Introduction to OSIS
- Our Mission & What We Do
- Alternative Approaches in the Face of the Pandemic
- Metrics

Organization Chart



Office of Study Integrity & Surveillance

Our Mission

- OSIS promotes the public health by ensuring the welfare of study subjects and by verifying the quality, study integrity and regulatory compliance of bioavailability/bioequivalence (BA/BE), nonclinical (GLP), and animal rule (AR) studies.

What We Do

Support FDA's and CDER's missions to protect the public health by:

- Conducting comprehensive study-directed and surveillance inspections of firms that conduct studies in support of human drug applications.

What We Do

Support FDA's and CDER's missions to protect the public health by:

- Developing and refining strategies to:
  - improve inspection planning, execution, and evaluation
  - provide recommendations to CDER review divisions, while focusing on human subject safety and data integrity.

What We Do

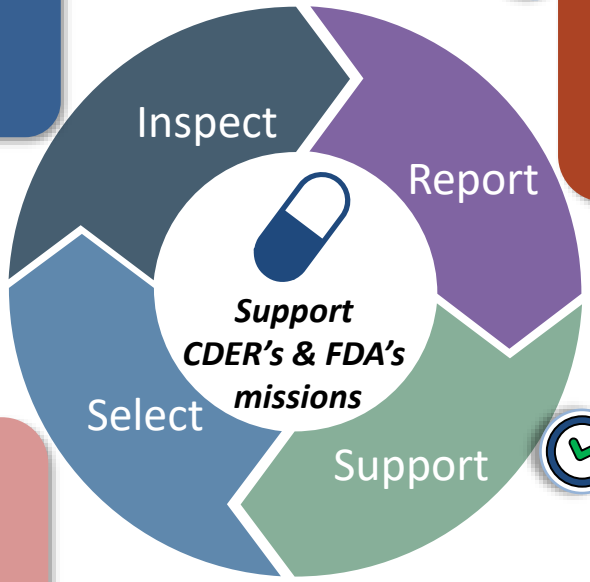
Support FDA's and CDER's missions to protect the public health by:

- Conducting outreach through:
  - participation in national and international conferences and workshops
  - collaborating with international regulatory agencies

OSIS Mission: Select, Inspect, Report, Support

Inspect sites to ensure quality and integrity of studies

Report on inspections by writing Establishment Inspection Reports and EIR Reviews



Select sites for inspection through surveillance evaluation and site assessment

Support CDER with data reliability recommendations and compliance evaluations

Inspection Process

Pre-inspection	Distribute workload between the team and prepare for the inspection.
Opening	Arrive to site unannounced & conduct opening meeting with the site.
Document Requests	Request the specific documents related to the study/studies under audit during the inspection
Facility Tour	Includes sample receipt & storage areas, laboratories, clinical facilities, archives, server room
Document Review	Discuss any concerns with the site & collect exhibits
Close out	Conduct a close out meeting with the site & issue a form FDA 483, if applicable

What do we cover during an inspection?

- Facilities & Site Operations
- Sample Storage Areas
- Instrument Calibration & Maintenance
- Data Security
- Sample Receipt & Accountability
- Reserve Samples
- SOPs
- Training Records
- Method Validations
- Precision & Accuracy
- Stability Assessments
- Recovery
- Sample Processing
- Sample Analysis
- Method Performance
- Audit Trails
- Documentation

Challenge Question #1

What role does OSIS play in the Drug Life Cycle?

A. Provide guidance and regulatory oversight to industry on a wide variety of clinical, scientific, and regulatory matters relating to generic drugs

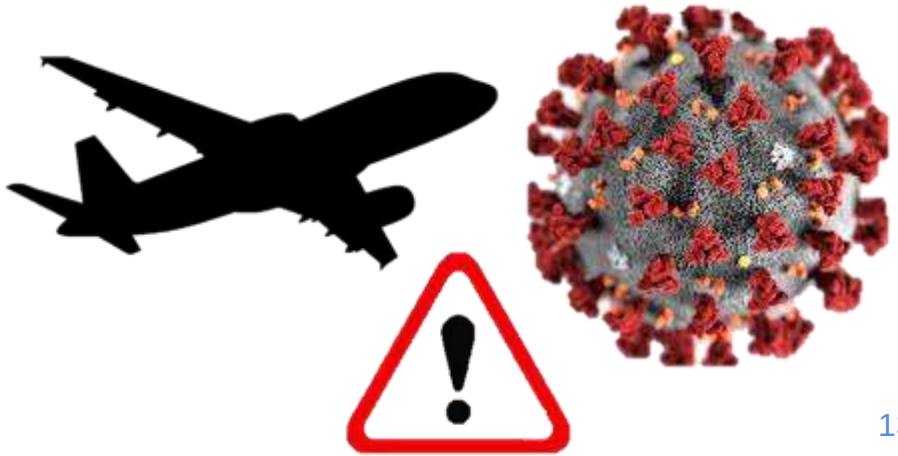
B. Conduct study-directed and comprehensive surveillance inspections of firms that conduct bioavailability/bioequivalence (BA/BE) and Good Laboratory Practice (GLP) studies sometimes with ORA investigators in support of human drug applications.

C. Conduct research to expand our knowledge of clinical pharmacology to better evaluate benefit and risk

D. Protect the public health by applying statistical approaches for monitoring the effectiveness and safety of marketed drugs and therapeutic biologic products.

COVID-19 Pandemic

- As a result of the COVID-19 global pandemic, routine on-site inspections were not possible due to travel restrictions (March 2020)
- All scheduled inspection travels were cancelled as of March 2020



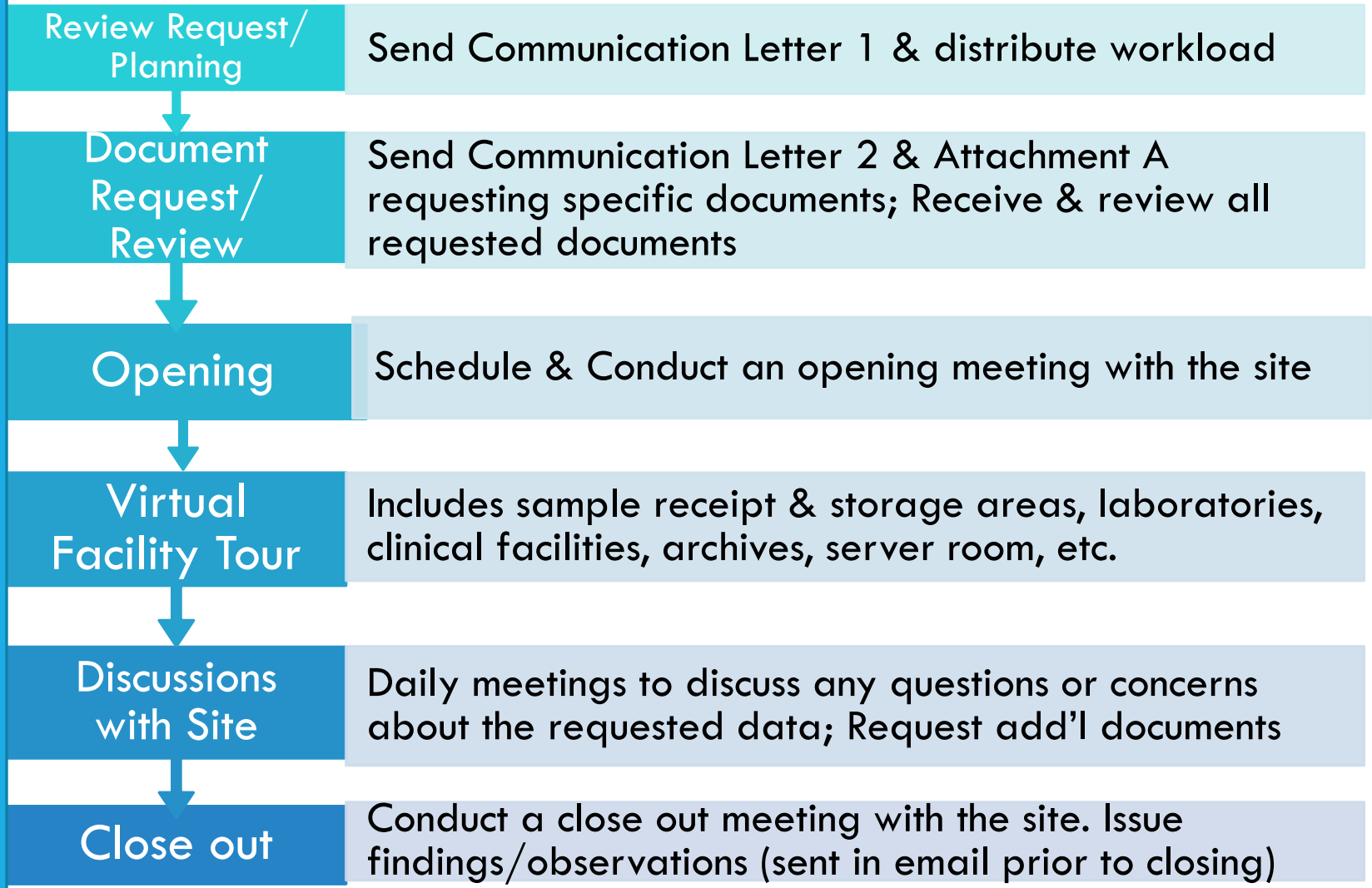
Alternative Approaches

- Remote Record Review
  - Tool established by OSIS to support CDER application assessments for certain products and situations, including when Agency travel is restricted
  - Rolled out June 2020
  - Similar to on-site inspections
  - Voluntary interaction with a site of interest

Remote Record Review

- Audit source records and documentation
- Communicate with site's staff
- Visualize electronic systems
- Observe certain areas of site's facility
- Any identified findings are discussed during the virtual interactions

Remote Record Review Process

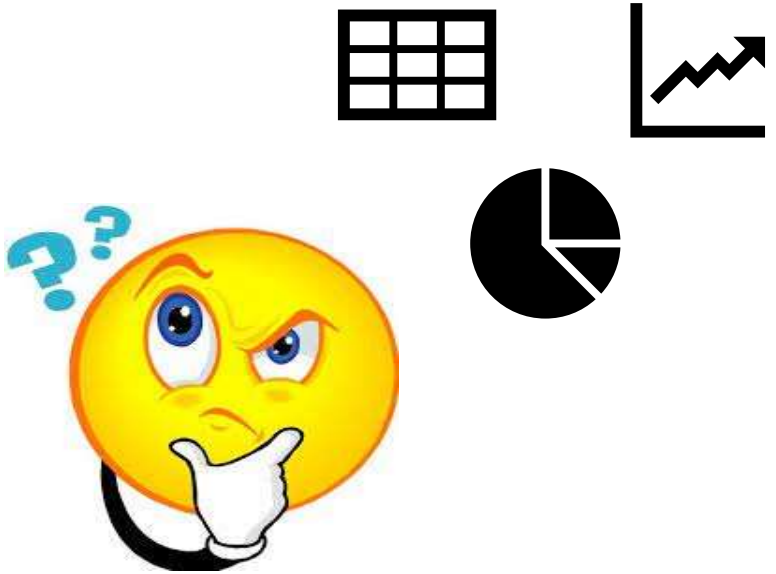


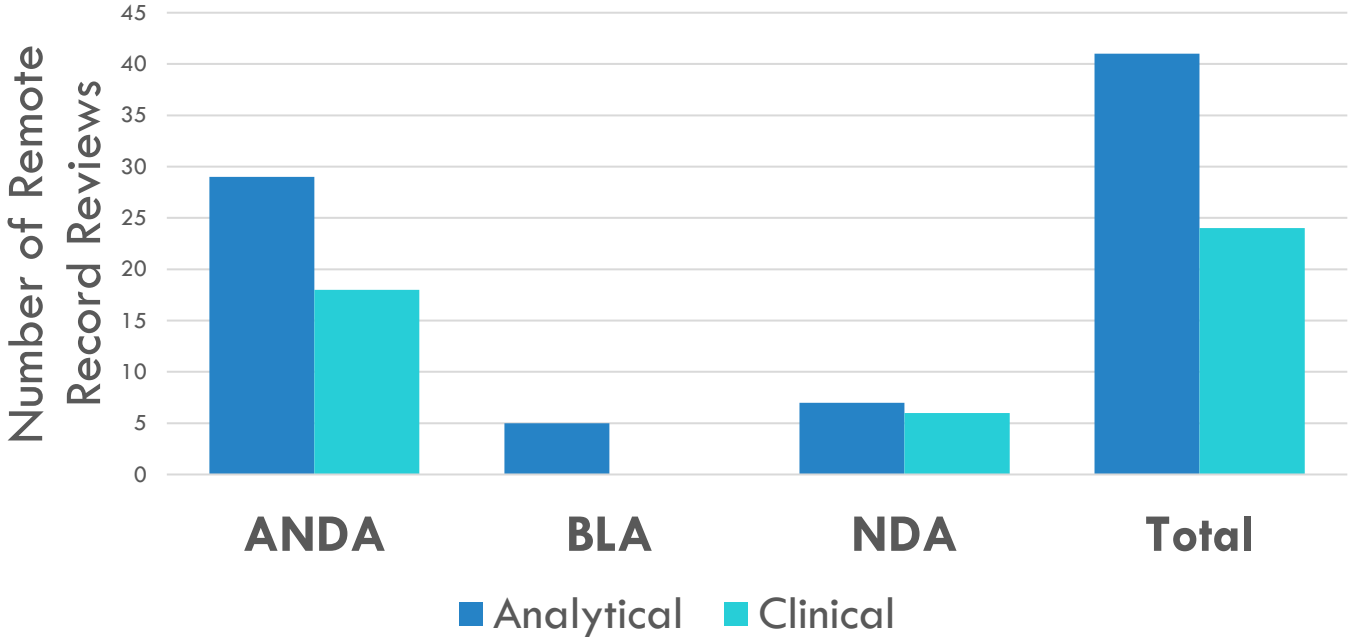
Records Reviewed include:

- Facilities & Site Operations
- Drug Product & Subject Sample Accountability (storage, handling & processing)
- Reserve Samples
- SOPs, Protocols & Protocol Deviations
- Training Records
- Method Validations & Sample Analysis
- Method Performance
- Audit Trails & Data Security
- Instrument Calibration & Maintenance
- Documentation
- AE reporting, Monitor Reports & IRB/IEC oversight (clinical)

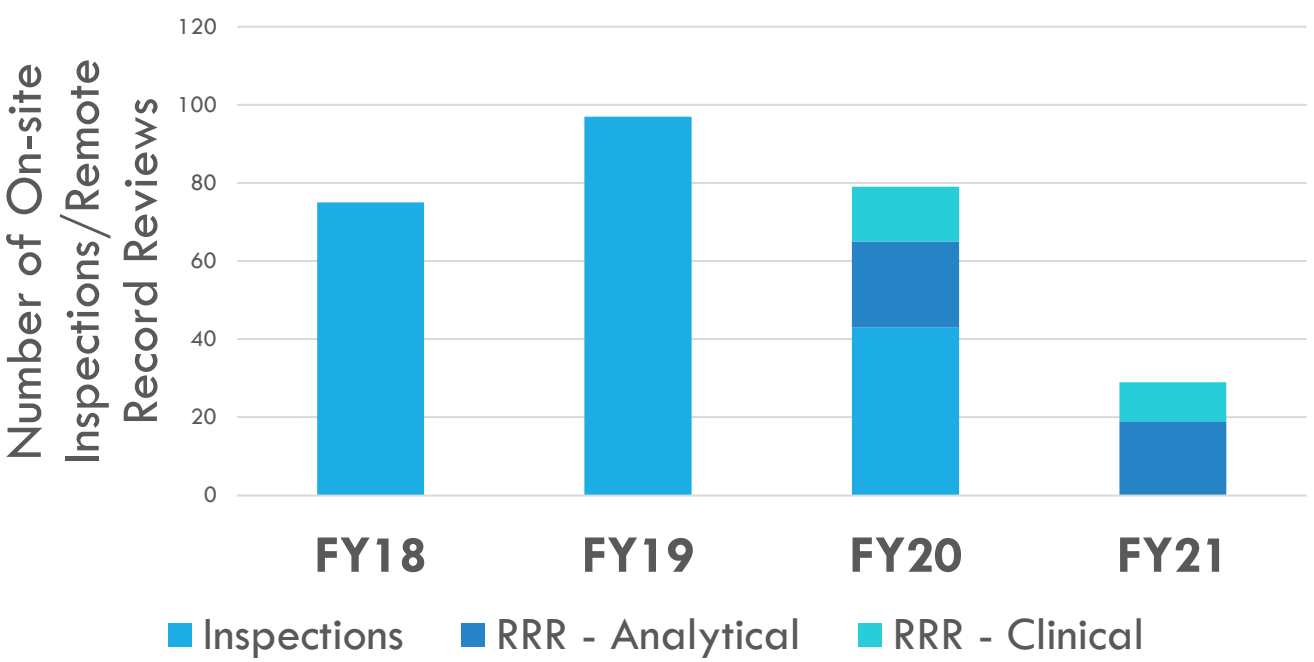
What do the numbers say?

Metrics





OSIS CONDUCTED REMOTE RECORD REVIEWS (since June 2020)



ON-SITE INSPECTIONS/REMOTE RECORD REVIEWS CONDUCTED BY OSIS

Challenge Question #2

A remote record review is NOT like an inspection because of the following reason:

A. It is voluntary process

B. Different aspects are covered

C. Written observations are not provided

D. There is no interview of the site's staff

Summary

- OSIS Mission
- OSIS's adaptation & innovation in face of Pandemic: Remote Record Review
- Metrics and how it compared to on-site inspections

Closing Thought

Despite the sudden travel related restrictions due to the COVID-19 pandemic,

OSIS quickly adapted and applied innovation in order to persevere in the continuation of our important work to fulfill our mission of helping to ensure public health/safety

Questions?

Makini K. Cobourne-Duval, Ph.D.
Pharmacologist
Office of Study Integrity and Surveillance (OSIS)
Office of Translational Sciences
Center for Drug Evaluation and Research (CDER) | US FDA

Generic Drugs Forum 2021: Lifecycle of a Generic Drug – April 28-29, 2021


FDA
U.S. FOOD & DRUG
ADMINISTRATION