Version 4 – Updated July 12, 2022

Office of Study Integrity and Surveillance Workshop 2022:

CDER Inspections of Good Laboratory Practice, Animal Rule, and Bioavailability/Bioequivalence Study Sites

For files and resources, please visit
The Event Page on SBIAevents.com

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AGENDA

All times are Eastern (EST UTC-4)

View Start Time on World Clock

DAY ONE: Tuesday, July 19, 2022

9:00 – 9:15

SBIA Welcome

Brenda Stodart, PharmD, MS, BCGP, RAC-US
Captain, United States Public Health Service
Director, Small Business, and Industry Assistance (SBIA)
Division of Drug Information (DDI) | Office of Communications (OCOMM) | CDER

9:15 – 9:20

Welcome by Office of Study Integrity and Surveillance (OSIS)

Sean Kassim, PhD
Director
Office of Study Integrity and Surveillance (OSIS)
Office of Translational Sciences (OTS) | CDER

9:20 – 9:30

Keynote

ShaAvhrée Buckman-Garner, MD, PhD
Director
Office of Translational Sciences (OTS) | CDER

9:30 – 9:45

OSIS - Introduction, Mission, Vision

This presentation will provide an overview of the mission, vision and role of OSIS in overseeing the Good Laboratory Practice, Animal Rule, and Bioavailability/ Bioequivalence Compliance Programs.

Tahseen Mirza, PhD
Associate Director for Regulatory Affairs
OSIS | OTS | CDER

DAY ONE: Tuesday, July 19, 2022

Your SBIA Hosts for Day One

Forest "Ray" Ford, PharmD, BCPS
Captain, USPHS
DDI | OCOMM | CDER

Renu Lal, PharmD
Lieutenant Commander, USPHS
DDI | OCOMM | CDER

Nora Lim, PharmD, BCPS
Lieutenant, USPHS, *Pharmacist*
SBIA | DDI | OCOMM | CDER

Session One: Overview of Good Laboratory Practice (GLP) Regulations and Compliance Programs (CPs)

9:45 – 10:05

Good Laboratory Practice (GLP) 101 - Regulation and Basic Studies

The importance of nonclinical laboratory studies to FDA's public health decisions demands that they be conducted according to scientifically sound protocols and with meticulous attention to quality. FDA established the Good Laboratory Practice (GLP) Regulations, 21 CFR Part 58, in 1979. This presentation will briefly go over the regulations and established standards for the conduct and reporting of nonclinical laboratory studies and are intended to assure the quality and integrity of safety data submitted to FDA.

Zhou Chen, MD, PhD
Team Lead, GLP Team
Division of New Drug Study Integrity (DNDSI)
OSIS | OTS | CDER

10:05 – 10:25

GLP Compliance Program

The instructor will provide an overview of the Good Laboratory Practice (GLP) (Nonclinical Laboratories) Compliance Program (CP) which is part of the FDA BIMO Program. Objective of the CP is

- to verify the quality and integrity of data submitted in a research or marketing application.
- to inspect (periodically) nonclinical laboratories conducting safety studies that are intended to support applications for research or marketing of regulated products.
- to audit safety studies and determine the degree of compliance with GLP regulations.

Erin McDowell
Biologist
DNDSI | OSIS | OTS | CDER

10:25 – 10:45

Inspection of Nonclinical Laboratories Conducting Animal Rule Specific Studies Compliance Program

FDA regulations that provide a pathway for approval of drugs and licensure of biological products when human efficacy studies are not ethical or feasible are commonly referred to as the Animal Rule. The Animal Rule applies to drugs or biological products developed to reduce or prevent serious or life-threatening conditions caused by exposure to lethal or permanently disabling toxic chemical, biological, radiological or nuclear substances, when human efficacy studies are not ethical, and field trials after accidental or deliberate exposure are not feasible. The inspections under this compliance program are conducted to verify, to the extent practicable, the quality and integrity of the data contained in final reports of Animal Rule-specific studies submitted to FDA. From this session, the attendees will learn about specifics of the Animal Rule CP.

Lynda Lanning, DVM, DABT
Biologist, GLP Team
DNDSI | OSIS | OTS | CDER

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DAY ONE: Tuesday, July 19, 2022

10:45 – 11:05

GLP Related Guidance Update: Pathology Peer Review and Whole Slide Imaging

Attendees will receive an update regarding two recently published Q&A guidances.
1. *Pathology Peer Review.* This question-and-answer document is intended to clarify FDA's recommendations concerning the management, conduct, and documentation of pathology peer review.
2. *Whole Slide Imaging*. This guidance provides information to sponsors and nonclinical laboratories regarding the use and management of whole slide images used during histopathology assessment and/or pathology peer review performed for good laboratory practice (GLP)-compliant nonclinical toxicology studies using non-human specimens.

Lynda Lanning, DVM, DABT
Biologist, GLP Team
DNDSI | OSIS | OTS | CDER

11:05 – 11:15: BREAK

11:15 – 11:30

Session One Questions & Answer Panel

Sean Kassim, Tahseen Mirza, Zhou Chen, Erin McDowell, Lynda Lanning

Session Two: Overview of OSIS BA/BE Program - Types of Studies

11:30 – 11:50

Bioavailability (BA) and Bioequivalence (BE) Studies supporting NDAs under the 505(b)(2) and ANDA under the 505(j) Application Pathways

This presentation provides an overview of the in vivo bioequivalence (BE) and bioavailability (BA) studies submitted to FDA to support NDAs and ANDAs through various regulatory pathways.

Yiyue (Cynthia) Zhang, PhD, RAC
Senior Staff Fellow, BE Team
DNDSI | OSIS | OTS | CDER

11:50 – 12:40: LUNCH BREAK

12:40 – 1:00

In Vitro BE Studies

This presentation provides an overview of commonly-used in vitro BE approaches for determining product BE. It will also elaborate on the principles for using in vitro release methods and product physicochemical understanding as a mechanism for assessing product BE for non-systemically absorbed dosage forms.

Monica Javidnia, PhD
Staff Fellow, BE Team
Division of Generic Drug Study Integrity (DGDSI)
OSIS | OTS | CDER

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DAY ONE: Tuesday, July 19, 2022

1:00 – 1:20

Immunogenicity

A major problem with protein-based therapeutics is their immunogenicity, that is, their tendency to trigger an unwanted immune response against themselves. One form of immune response results in the production of antibodies that bind to the proteins and reduce or eliminate their therapeutic effects. Such antibodies can also cause complications that can be life-threatening. Therefore, a critical part of determining the clinical safety and efficacy of protein-based therapeutic products is measuring their tendency to trigger antibody formation. This session will provide a brief introduction to the concept of immunogenicity response of therapeutics.

Kara Scheibner, PhD
Pharmacologist, BE Team
DGDSI | OSIS | OTS | CDER

1:20 – 1:35

Session Two Questions & Answer Panel

Yiyue (Cynthia) Zhang, Monica Javidnia and **Kara Scheibner**

Session Three: Overview of Clinical BA/BE Inspections - Clinical Compliance Program

This Compliance Program (CP) entitled 'Procedures for FDA Staff: In Vivo Bioavailability/Bioequivalence Studies (Clinical)' outlines procedures for FDA investigators who inspect domestic or international sites to ensure that the clinical portions of in vivo bioavailability (BA) and bioequivalence (BE) studies, including studies with pharmacokinetic (PK), pharmacodynamic (PD), or clinical endpoints (CE) submitted to the Center for Drug Evaluation and Research (CDER), are conducted in a manner that ensures subject safety and data integrity, and to document study conduct in accordance with applicable regulations. This CP is designed to ensure studies are conducted using the highest laboratory standards and in accordance with applicable regulations.

1:35 – 1:55

Inspecting Clinical BA/BE Studies

The presenter will discuss the inspectional approach for the clinical portion of the in vivo BA/BE studies as described in the CP above.

Xingfang Li, MD, RAC
Pharmacologist, BE Team
DGDSI | OSIS | OTS | CDER

1:55 – 2:15

Inspecting BE Studies with Clinical Endpoints

The presenter will discuss the inspectional approach for the BE Studies with Clinical Endpoints.

Xikui Chen, PhD
Pharmacologist, BE Team
DGDSI | OSIS | OTS | CDER

2:15 – 2:35

Overview of Reserve Samples

This presentation will cover procedures for handling reserve samples from relevant bioavailability (BA) and bioequivalence (BE) studies, as required by 21 CFR 320.38 and 320.63,[2] and the expectations regarding responsibilities of each party involved in the study pertaining to reserve samples.

Li-Hong Yeh, PhD
Interdisciplinary Scientist, BE Team
DNDSI | OSIS | OTS | CDER

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DAY ONE: Tuesday, July 19, 2022

2:35 – 2:45

Session Three Questions & Answer Panel

Xingfang Li, Xikui Chen, and **Li-Hong Yeh**

2:45 – 2:55: BREAK

Session Four: Overview of Analytical BA/BE Inspections - Analytical Compliance Program

This Compliance Program (CP) entitled 'Procedures for FDA Staff: In Vivo Bioavailability/Bioequivalence Studies (Analytical)' outlines procedures for FDA investigators who inspect domestic and international sites to ensure that the analytical portions of in vivo bioavailability (BA), bioequivalence (BE), pharmacokinetic (PK), or pharmacodynamic (PD) studies submitted to the FDA are conducted using the highest laboratory standards and in accordance with applicable regulations. This CP is designed to ensure studies are conducted using the highest laboratory standards and in accordance with applicable regulations.

2:55 – 3:15

In Vivo Studies

The presenter will discuss the inspection of the analytical portion of the in vivo BA/BE studies as described in the CP above.

Gopa Biswas, PhD
Team Lead, BE Team
DNDSI | OSIS | OTS | CDER

3:15 – 3:35

In Vitro Studies

This session will go over the inspection approach for in vitro studies that may be used in lieu of in vivo studies as outlined CFR 21 Part 320.

Sripal Mada, PhD
Pharmacologist, BE Team
DNDSI | OSIS | OTS | CDER

3:35 – 3:55

Immunogenicity Studies

The objective of this presentation is to go over the inspectional approach for analytical studies and assays that determine immunogenicity of therapeutic moieties.

Kara Scheibner, PhD
Pharmacologist, BE Team
DNDSI | OSIS | OTS | CDER

3:55 – 4:05

Session Four Questions & Answer Panel

Gopa Biswas, Sripal Mada, and **Kara Scheibner**

4:05 – 4:10

Day One Closing

Brian Folian, MS, JD
Deputy Office Director
OSIS | OTS | CDER

4:10: DAY ONE ADJOURN

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DAY TWO: Wednesday, July 20, 2022

9:00 – 9:10

SBIA Welcome

Forest "Ray" Ford, PharmD, BCPS
Captain, USPHS
DDI | OCOMM | CDER

Renu Lal, PharmD
Lieutenant Commander, USPHS
DDI | OCOMM | CDER

Nora Lim, PharmD, BCPS
Lieutenant, USPHS, *Pharmacist*
SBIA | DDI | OCOMM | CDER

Day Two: Case Studies

The case studies in these sessions are designed for audience participation in resolving situations (cases) confronted by OSIS during inspection of sites. The purpose of the case studies is to emphasize the principles learned during the workshop. The instructor will present detailed scenarios based on OSIS's inspectional experience. This will be followed by questions for consideration by the participants. Then the participants will be encouraged to share their thoughts and answers. The instructor will triage the answers and also provide the 'correct' answers at the end.

9:10 – 10:00

GLP Case Study

Lynda Lanning, DVM, DABT
Biologist, GLP Team
DNDSI | OSIS | OTS | CDER

Zhou Chen, MD, PhD
Team Lead, GLP Team
DNDSI | OSIS | OTS | CDER

10:00 – 10:50

Animal Rule Case Study

Lynda Lanning, DVM, DABT
Biologist, GLP Team
DNDSI | OSIS | OTS | CDER

Yiyue (Cynthia) Zhang, PhD
Senior Staff Fellow, BE Team
DNDSI | OSIS | OTS | CDER

10:50 – 11:00: BREAK

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DAY TWO: Wednesday, July 20, 2022

11:00 – 11:50

Clinical BA/BE Case Study

Doug Pham, PharmD, JD
Associate Director for Clinical Policy
OSIS | OTS | CDER

11:50 – 12:30: LUNCH BREAK

12:30 – 1:20

Analytical BA/BE Case Study

Sarmistha Sanyal, PhD
Chemist, BE Team
DGDSI | OSIS | OTS | CDER

1:20 – 2:10

In Vitro BE Case Study

Gajendiran Mahadevan, PhD
Pharmacologist, BE Team
DNDSI | OSIS | OTS | CDER

2:10 – 2:20: BREAK

2:20 – 3:10

Immunogenicity Case Study

Amanda Lewin, PhD
Team Lead, BE Team
DGDSI | OSIS | OTS | CDER

3:10 – 3:20

Day Two Closing

Sean Kassim, PhD
Director
Office of Study Integrity and Surveillance
OTS | CDER

3:20: ADJOURN

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