



Overview

Navigating Complex Waters: A Deep Dive into FDA Drug Interactions Guidances & Resources

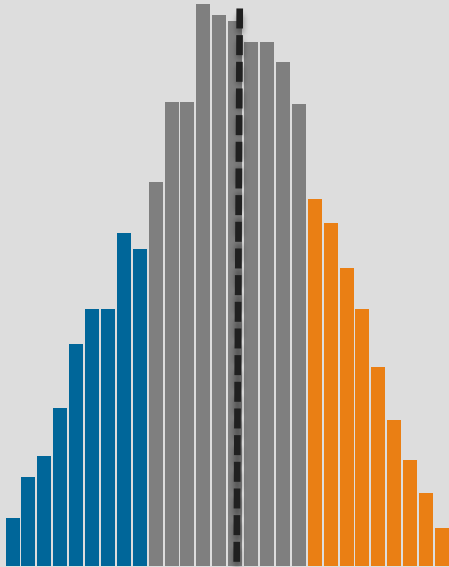
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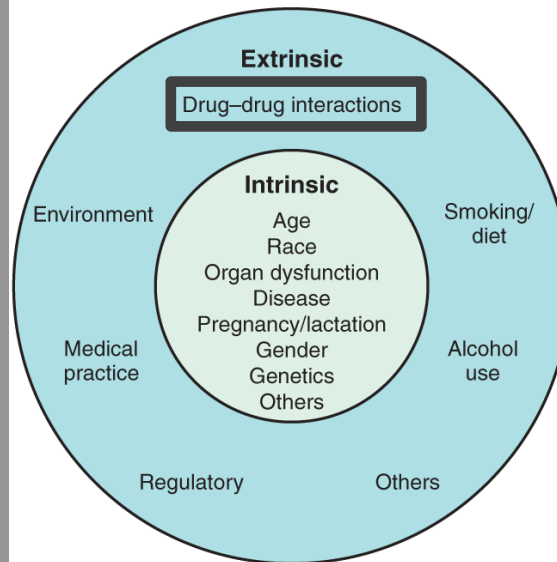


Heterogeneity in Drug Response & Therapeutic Individualization

Drug Response



Factors



Translation



Drug Interactions

- ▶ Drug interactions can occur when patients take more than one drug
 - May impact safety or efficacy resulting in altered benefit/risk
- ▶ The potential for drug interaction for new medicinal products should be evaluated.
 - Impractical to evaluate every drug interaction in clinical trials during new drug development
- ▶ Systematic risk-based strategies are essential to characterize drug interaction potential
 - Regulatory agencies have developed guidelines to assist drug developers



Drug Interactions - Guidance

In Vitro Drug Interaction Studies – Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions Guidance for Industry (2020)

Clinical Drug Interaction Studies - Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions Guidance for Industry (2020)

Physiologically Based Pharmacokinetic Analyses – Format and Content (2018)

Population Pharmacokinetics: Guidance for Industry (2022)

M12 Drug Interaction Studies ICH Harmonised Guideline Draft version (2022)

Clinical Pharmacology Labeling for Human Prescription Drug and Biological Products – Content and Format (2016)



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Drug Development and Drug Interactions | Table of Substrates, Inhibitors and Inducers

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Drug Interactions & Labeling

Drug Development and Drug Interactions | Table of Substrates, Inhibitors and Inducers

Drug Interactions | Relevant Regulatory Guidance and Policy Documents

Drug Development and Drug Interactions | Resources

- CYP Enzymes
 - In vitro
 - [In vitro marker reactions](#)
 - [In vitro selective inhibitors](#)
 - [In vitro inducers](#)
 - Clinical index drugs
 - [Clinical index substrates](#)
 - [Clinical index inhibitors](#)
 - [Clinical index inducers](#)
 - Examples of clinical substrates, inhibitors, and inducers
 - [Clinical substrates](#)
 - [Clinical inhibitors](#)
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- Transporters
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 - Examples of clinical substrates, inhibitors and inducers
 - [Clinical substrates](#)

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Regulated Product(s)
Drugs



Drug Interactions - Guidance

- ▶ Need to consider
 - Non-enzyme/transporter mediated interactions
 - Specific therapeutic context
 - Unique mechanistic aspects for biologics and emerging modalities
 - Resources tailored to support Healthcare Professionals

For Healthcare Professionals | FDA's Examples of Drugs that Interact with CYP Enzymes and Transporter Systems

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Drug Interactions & Labeling

Drug Development and Drug Interactions | Table of Substrates, Inhibitors and Inducers

Drug Interactions | Relevant Regulatory Guidance and Policy Documents

Drug Development and Drug Interactions | Resources

On this page

- [CYP Enzyme- and Transporter System-Based Clinical Substrates, Inhibitors, or Inducers](#)
- [Legend](#)

Drug-drug interactions can lead to changes in systemic exposure (e.g., maximum concentration (C_{max}), area under the concentration time curve (AUC), average steady state concentration (C_{ps})) potentially resulting in adverse reactions (higher drug exposure) or loss of efficacy (lower drug exposure).

Cytochrome P-450 (CYP) enzymes are responsible for the metabolism of many drugs, and transporter systems allow for movement of many drugs across cell membranes. Thus,

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06/05/2023

Regulated Product(s)
Drugs

Evaluation of Gastric pH-Dependent Drug Interactions With Acid-Reducing Agents: Study Design, Data Analysis, and Clinical Implications
Guidance for Industry (2023)

Clinical Drug Interaction Studies With Combined Oral Contraceptives
Guidance for Industry (2023)

Drug-Drug Interaction Assessment for Therapeutic Proteins
Guidance for Industry (2023)



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CDER SBIA Webinar, Dec 12-13, 2023