ICH M12 Drug Interaction Studies Final Guidance

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Objectives

- Introduction- Helen Heymann, MMSc

- In Vitro DDI Assessments - Xinning Yang, PhD
  - Q&A / Panel

- Clinical DDI Assessments – Kellie Reynolds, PharmD
  - Q&A / Panel:
    - Rajanikanth Madabushi, PhD
    - Kellie Reynolds, PharmD
    - Xinning Yang, PhD
    - Helen Heymann, MMSc

Introduction Overview

- Rationale for Guidance
- Goal and Scope of Guidance
- Process and Timeline
- Implication of Adoption of ICH Guideline by FDA

Rationale for Guidance

- **Why focus on Drug Drug Interactions (DDIs)**
  - DDIs – taking more than one drug
  - Decrease risk of adverse events or loss of efficacy for patients
  - Risk based approaches for assessing DDIs

- **Why Globally Harmonize**
  - Differences between regions: inconsistent expectations /recommendations
  - International Council on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) as a convenor for harmonization
  - ICH DDI guideline developed through strong alignment among regional agencies

Approved Guidance Goal and Scope

- **Goal:** Harmonize recommendations on designing, conducting, and interpreting in vitro & clinical DDI studies during development of therapeutic product
- **Scope:** Assessment of pharmacokinetic drug interactions mediated by metabolic enzymes and drug transporters

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Scope	**Out-of-scope**
pharmacokinetic interactions (enzyme and transporter mediated)	pharmacodynamic and kinetic interactions (gastric pH change and formation or complexes or chelates; food effect);
small molecules and biologic products (monoclonal antibodies; antibody-drug conjugates)	new modalities (oligonucleotides)

ICH Guideline Development Process and Timeline

Path to ICH M12 Guideline Harmonization & Delivery

ICH Step 1: Consensus Building On Technical Document (June 2018-November 2019)

9 Regulatory Agencies

6 Industry Organizations

ICH Guideline Development Process and Timeline

Path to ICH M12 Guideline Harmonization & Delivery

ICH Step 2A: ICH Parties Consensus on M12 Technical Document (May 2020-Nov. 2021)

ICH Step 1: Consensus Building On Technical Document (June 2018-November 2019)

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ICH Guideline Development Process and Timeline

Path to ICH M12 Guideline Harmonization & Delivery

ICH Step 2B: Draft M12 Guideline Adoption by Regulators (June 2022)

ICH Step 2A: ICH Parties Consensus on M12 Technical Document (May 2020-Nov. 2021)

ICH Step 1: Consensus Building On Technical Document (June 2018-November 2019)

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ICH Guideline Development Process and Timeline

Path to ICH M12 Guideline Harmonization & Delivery

- ICH Step 3: Regulatory Consultation & Discussion (November 2022-November 2023)
- ICH Step 2B: Draft M12 Guideline Adoption by Regulators (June 2022)
- ICH Step 2A: ICH Parties Consensus on M12 Technical Document (May 2020-Nov. 2021)
- ICH Step 1: Consensus Building On Technical Document (June 2018-November 2019)

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ICH Guideline Development Process and Timeline

Path to ICH M12 Guideline Harmonization & Delivery

- **ICH Step 4: Adoption of ICH M12 Harmonized Guideline (March 2024)**
- **ICH Step 3: Regulatory Consultation & Discussion(November 2022-November 2023)**
- **ICH Step 2B: Draft M12 Guideline Adoption by Regulators (June 2022)**
- **ICH Step 2A: ICH Parties Consensus on M12 Technical Document (May 2020-Nov. 2021)**
- **ICH Step 1: Consensus Building On Technical Document (June 2018-November 2019)**

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ICH Guideline Development Process and Timeline

Path to ICH M12 Guideline Harmonization & Delivery

- ICH Step 5: M12 Guideline Implementation (May 2024 and beyond)
- ICH Step 4: Adoption of ICH M12 Harmonized Guideline (March 2024)
- ICH Step 3: Regulatory Consultation & Discussion(November 2022-November 2023)
- ICH Step 2B: Draft M12 Guideline Adoption by Regulators (June 2022)
- ICH Step 2A: ICH Parties Consensus on M12 Technical Document (May 2020-Nov. 2021)
- ICH Step 1: Consensus Building On Technical Document (June 2018-November 2019)

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What is the implication for FDA's 2020 Guidances?

- **ICH Guideline adopted as of August 2024 replaces the January 2020 final guidances for industry:**
  - In Vitro Drug Interaction Studies — Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions
  - Clinical Drug Interaction Studies — Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions

Current Final FDA Guidance accessible at:

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/m12-drug-interaction-studies


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