Scientific Harmonization of Bioequivalence Standards for Generic Drugs

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Learning Objectives

- Delineate strategies proposed in the ICH Reflection Paper on "Further Opportunities for Harmonization of Standards for Generic Drugs"
- Provide an update on new developments in ICH since the publication of the ICH Reflection Paper
- Describe FDA's role in leading ICH activities for developing and enhancing ICH guidelines to support the harmonization of scientific and technical standards for generic drugs

ICH: The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ich.org)

Global Harmonization for Generic Drugs

- Generic drugs comprise a significant portion of the pharmaceutical market
- Common standards for global development for generics can improve access to generic medicines
- ICH is uniquely positioned to develop harmonized recommendations as the global venue for harmonization of standards for pharmaceutical products
  - Regulatory members are expected to implement ICH guidelines
- Historically, ICH has focused on standards for new drugs, however, many ICH guidelines are applicable to generic drugs (e.g., ICH Quality Guidelines)

What are the strategies for developing and enhancing ICH guidelines to support the harmonization of scientific and technical standards for generic drugs?

ICH Reflection Paper on Generic Drug Harmonization

- Outlines a strategic approach for developing and enhancing ICH guidelines to support the harmonization of scientific and technical standards for generic drugs
- Proposes steps and recommendations for global harmonization of standards for generic drugs
- The reflection paper (drafted by FDA) was discussed at the November 2018 ICH Assembly Meeting and endorsed by ICH

https://admin.ich.org/sites/default/files/2019-04/ICH_ReflectionPaper_GenericDrugs_Final_2019_0130.pdf

Key Proposals in the Reflection Paper

- Develop a series of ICH guidelines on standards for demonstrating equivalence (e.g., bioequivalence) for
  - Non-complex dosage forms
  - More complex dosage forms and products

- Establish a generic drug discussion group
  - To assist in assessing the feasibility of harmonization of standards for generic drugs
  - To prioritize work areas

Regulatory and Scientific Frameworks for Generic Drugs

- The reflection paper recognizes that different regions have different regulatory frameworks
  - Example: Tablet and Capsule
    - Not a “generic” in the United States
    - Possible “generic” in the EU
- The reflection paper focuses on harmonizing scientific standards for bioequivalence that can be used within the existing regulatory frameworks

Reflection Paper Outcomes (1)

- Formed an ICH Generic Drug discussion Group (GDG) in April 2019
  - One-year remit*
    - Rapporteur: Dr. Nilufer Tampal (FDA, United States)
    - Regulatory Chair: Dr. Jan Welink (European Commission, Europe)
  - To assist ICH in identifying recommended topic areas for harmonization
  - To survey existing ICH and World Health Organization (WHO) guidelines to assess gaps in guidances for generic drugs
  - To prioritize work areas and send proposals/make recommendations to ICH

* https://database.ich.org/sites/default/files/IGDG_Remit.pdf

Reflection Paper Outcomes (2)

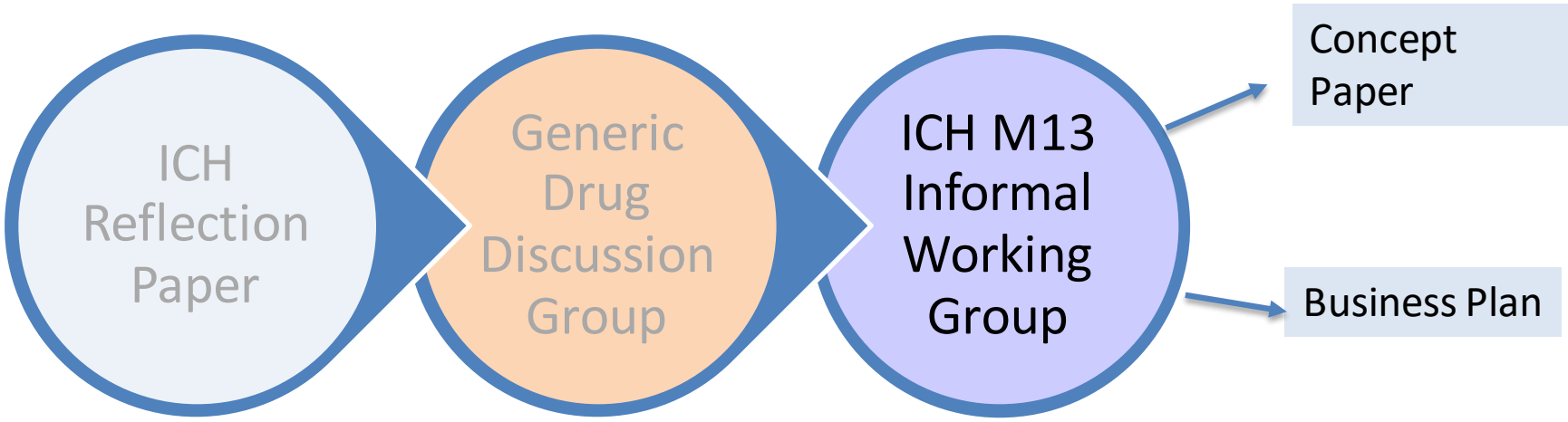
GDG Main Tasks:

- Finished information sharing and reached a consensus within the GDG on the scope of the ICH topic proposal on an initial guideline on "Bioequivalence for Immediate-Release Solid Oral Dosage Forms"
- Finalized and submitted the revised ICH topic proposal to ICH Management Committee (MC)
- Conduct Tasks 1 and 2 according to the GDG work plan
  - **Task Group 1:** GDG should identify additional topics for subsequent harmonization or a potential bioequivalence (BE) guideline series
  - **Task Group 2:** GDG should assess the existing ICH guidelines (e.g., Multidisciplinary and Efficacy guidelines) to identify any need for revision.

Will be completed in April 2020

Reflection Paper Outcomes (3)

- First ICH Topic on Bioequivalence Harmonization was endorsed by ICH Assembly in November 2019
  - ICH M13: "Harmonization of BE standards for immediate-release oral dosage forms"
  - Informal Working Group was formed in February 2020
    - Rapporteur: Dr. Lei Zhang (FDA, United States)
    - Regulatory Chair: Dr. Jan Welink (European Commission, Europe)
  - Goal: Complete concept paper and business plan in May-June 2020



Potential Future Areas

- Issues related to more complex products may be on the horizon
  - Modified-release products
  - Complex Injectables
  - Transdermal
  - Topical dermatological
  - Inhalation

Value of Scientific Harmonization

- Bioequivalence studies worldwide can be conducted according to common expectations
  - Increases efficiency of generic drug development
  - Increases quality of generic drug development
- It is the essential first step toward global development of generic products

What Are the Opportunities?

- Movement toward common standards for global development for generics can improve access to generic products
  - Products with small markets may not be economically viable unless markets can be aggregated across regions
  - Investment in development of complex generics can be supported by entrance into multiple markets

What Are the Challenges?

- What are the scientific data and analytical tools that provide evidence that reference product sourced in region “A” and reference product sourced in region “B” are similar enough that BE comparisons will be the same?
  - ICH expert working group
- A regulatory policy system in each region that will allow scientifically sound data to be used
  - Regulatory members

What Is the Role of Industry?

- Invest in research and development
- Participate in ICH expert working groups
  - Share relevant data on regulatory and scientific challenges
  - Provide useful input into ICH discussions
  - Address challenges to lead towards harmonization in standards

Summary

- Generic drugs comprise a significant portion of the pharmaceutical market, and common standards for global development for generics can improve access to generic medicines
- ICH is uniquely positioned to develop harmonized recommendations as the global venue for harmonization of standards for pharmaceutical products
- ICH reflection paper on "Further Opportunities for Harmonization of Standards for Generic Drugs" lays out the strategy for global harmonization for generic drugs
- ICH M13 will be developed to harmonize BE standards for Immediate-Release oral dosage form drugs
- Discussion of harmonization will lead to global standards for generic product equivalence

Challenge Question

- A new guideline for harmonizing bioequivalence standards for immediate-release solid oral dosage form drugs will be developed under ICH.

a. True

b. False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