Introduction to Regulatory Considerations for MPTs

Charu Mullick, MD
Division of Antiviral Products,
Center for Drug Evaluation and Research, FDA
Multipurpose Preventive Technologies Symposium
January 11-12, 2012
Overview

• Terminology
  – What is a Combination Product?
  – What is a Multi-Indication Product?

• FDA jurisdiction for Combination Products

• Considerations pertinent to Combination Products
Terminology

• Combination Products [21 CFR 3.2 (e)]
  – Products comprised of differently regulated constituent parts i.e., drug, device, biologic product
    • Physically or chemically combined into one entity
    • Co-packaged entities intended for use together
    • Including two or more active drugs in combination
Terminology

• Product with more than one indication
  – Product intended to be effective for the treatment or prevention of different diseases or conditions
  – Examples
    • Single active agent
      – Tenofovir is approved for HIV treatment and Hepatitis B treatment
    • Two or more active agents which are individually active for separate indications and combined into one product
      – Sitagliptin and simvastatin fixed-dose combination
      – Both components were previously approved separately
Product Jurisdiction at FDA

• Depending on constituent parts, a product may be reviewed by different Centers at FDA
  - CDER, Center for Drug Evaluation and Research – Drug products
  - CBER, Center for Drug Evaluation and Research – Biologics
  - CDRH, Center for Devices and Radiological Health – Devices

• Review of a combination product
  - FDA’s Office of Combination Products (OCP) assigns one Center to have primary jurisdiction for the combination
  - Assignment decision is based on product’s primary mode of action
  - Refer to FDA Guidance: Early Development Considerations for Innovative Combination Products (Sept. 2006)
Two or More Unmarketed Drugs Developed for Use in Combination

- FDA has issued a guidance for developing two or more investigational drugs for one indication
  - FDA-CDER Guidance for Industry: Co-development of Two or More Unmarketed Investigational Drugs for Use in Combination (draft Dec 2010)

- Guidance outlines situations where co-development is an acceptable option

- Efficacy of each investigational agent should be demonstrated separately and together
Two or More Unmarketed Drugs Developed for Use in Combination

• Safety Considerations
  – Preclinical Safety
    • Toxicology studies carried out for separate drugs is considered sufficient to support first in human study with the combination product

• Refer to ICH guidance on Nonclinical Safety Studies
  – Guidance for Industry: M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization, January 2010
Two or More Unmarketed Drugs Developed for Use in Combination

• Safety Considerations (contd.)
  – Clinical Safety
    • If investigational agents are unmarketed
      – Safety profile of each individual drug should be characterized in phase 1 studies (similar to what would be done for development of a single drug)

• If an investigational agent in the combination is already approved
  – Sponsors may rely on existing safety data for the approved component provided the same formulation, dose, dosing schedule, delivery method is being pursued in the combination product
Other Considerations

• For a product being developed for two or more indications, the FDA does not designate one indication as primary or secondary
  – FDA experts in the specific field will provide review for each indications sought

• Sponsors are encouraged to submit different IND (investigational new drug) applications for each proposed development indication
  – To simplify managing communications and submissions for each indication pursued
Conclusion

• The FDA recognizes the development of multi-indication combination products will involve unique regulatory considerations.

• Regulatory challenges, considerations, and decisions will be product-specific as well as indication-specific.

• The FDA encourages initiating contact and discussion for combination products early in the development program.