FDA Public Workshop

Mechanistic Oral Absorption Modeling and Simulation for Formulation Development and Bioequivalence Evaluation

Docket Number FDA-2016-N-0668

May 19, 2016

Building 31 Great Room 1503 B and C

Agenda

8:00 – 8:30 am	**Registration**
8:30 – 8:35 am	**Welcome and Logistics** Liang Zhao, PhD, Director, FDA/OMPT/CDER/OGD/ORS/DQMM
8:35 – 8:45 am	**Opening Remarks** Kathleen (Cook) Uhl, MD, Director, FDA/OMPT/CDER/OGD
8:45 – 9:00 am	**Introduction and Objectives of the Workshop** Liang Zhao, PhD, Director, FDA/OMPT/CDER/OGD/ORS/DQMM
9:00 – 9:25 am	**The Application of Mechanistic Oral Absorption Model in Biopharmaceutics Review** John Duan, PhD, Acting Branch Chief, FDA/OMPT/CDER/OPQ/ONDP/DB/BBIII
9:25 – 9:50 am	**OGD Experience and Efforts on Oral Absorption Modeling and Simulation** Xinyuan Zhang, PhD, Scientific Lead, FDA/OMPT/CDER/OGD/ORS/DQMM
9:50 – 10:15 am	**Break**
10:15 – 10:40 am	**Oral Absorption Modeling and Simulation for Formulation Development and Bioequivalence Evaluation: An Industry Perspective** Filippos Kesisoglou, PhD, Senior Principal Scientist, Merck, PQRI/BTC
10:40 – 11:05 am	**Modeling and Simulations for Development and Bioequivalence Evaluation of a Generic Drug Product** Jasmina Novakovic, PhD, Scientific Leader, Apotex
11:05 – 11:30 am	**Mechanistic Oral Absorption Modeling and Simulation for Formulation Development and Bioequivalence (BE) Evaluation** Gordon Amidon, PhD, The Charles R. Walgreen Jr. Professor, University of Michigan
11:30 am-12:30 pm	**Lunch** (not provided)
12:30 – 12:55 pm	**Mechanistic Modeling and Simulation of Oral Drug Absorption: Opportunities and Challenges** Masoud Jamei, PhD, Vice President of R&D, Simcyp (a Certara company)
12:55 – 1:20 pm	**Incorporating Mechanistic Modeling & Simulation to Assist with Formulation Development** Viera Lukacova, PhD, Team Leader, SimulationsPlus

1:20 – 1:45 pm	**PK-Sim for Mechanistic Oral Absorption Modeling and Simulation and More** Thomas Eissing, PhD, Head of Systems Pharmacology CV, Bayer Technology
1:45 – 2:10 pm	**OrBiTo: Innovative Tools for Oral Biopharmaceutics** Filippos Kesisoglou, PhD, on behalf of OrBiTo
2:10 – 2:30pm	**Break**
2:30 – 4:00 pm	Panel Discussion
4:00 – 4:30 pm	Questions and Comments from the Audience for Panel Discussion
4:30 – 4:40 pm	**Closing Remarks** Robert Lionberger, PhD, Director, FDA/ OMPT/CDER/OGD/ORS

Please be advised a transcript will be accessible upon availability at http://www.fda.gov/Drugs/NewsEvents/ucm488178.htm. Written and electronic comments will be accepted after the hearing until June 20, 2016, Docket Number FDA-2016-N-0668. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers lane, Rm. 1051, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov/.

Questions for panel discussion

1. For the following area(s), which one(s) do we have the highest confidence in using physiologically based absorption (PBPK absorption) modeling and simulations for oral dosage forms?
    - Identification of clinically relevant specifications for in vitro tests (such as dissolution), or critical quality attributes (such as particle size)
        a. Formulation /process specific specifications; are the specifications transferable across formulations manufactured using various manufacturing principles?
        b. Applicability across different release mechanisms (e.g. osmotic pump vs matrix)
    - Bioequivalent formulation design
        a. Characterization of the reference listed drug
    - Mechanistic understanding of in vitro in vivo correlations
    - Food effect prediction
    - Pharmacokinetics and/or Bioequivalence extrapolation to special populations (such as pediatric, elderly, or gastrointestinal disease populations)
    - Drug-drug interaction predictions
    - Excipient effect assessment on drug absorption
    - Assessment of in vivo alcohol dose dumping
    - Risk assessment for waiver of in vivo studies for different strengths
    - Risk assessment for new formulations with release mechanism changes
    - Explanation of the mechanistic basis of nonlinear pharmacokinetics for substrates of enzymes and influx and efflux transporters in the gastrointestinal tract
    - Outlier assessment
    - Identification of major sources of inter-subject variability

2. Do we have enough experience and confidence in applying the current physiologically based pharmacokinetic (PBPK) and absorption models to support the following regulatory applications?
    - Support particle size distribution specification for an immediate release drug product of a drug with a low solubility
    - Support dissolution specification for a modified release drug product
    - Support request to widen the BCS III biowaiver criteria (proposed longer dissolution time than very rapidly dissolve and/or different excipients)
    - Support in vitro-in vivo correlation of an API with less than three formulations with different release rates
    - Support new proposals to demonstrate bioequivalence for GI locally acting drug products
3. For the areas with middle to low confidence, what are the gaps and how to close the gaps through research?