Quantitative Methods and Generic Drugs: Current Approaches and Future Directions in Health Canada

FDA Public Workshop: Leveraging Quantitative Methods and Modeling to Modernize Generic Drug Development and Review. Silver Spring, MD, October 2-3, 2016

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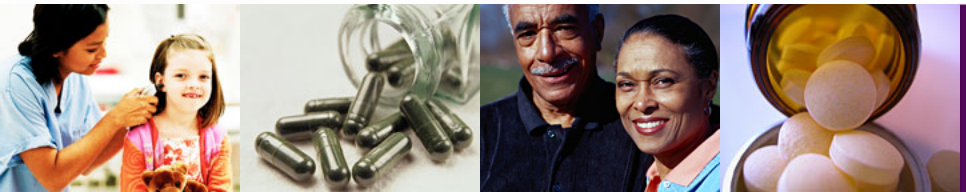
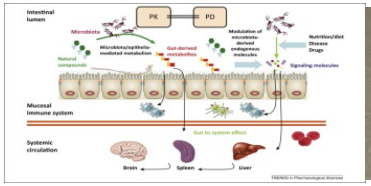
Canada

Disclaimer

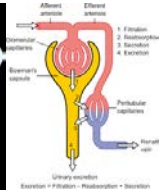
The scientific views and opinions expressed in this presentation are those of the speaker and do not necessarily represent the policy or recommendations of Health Canada.



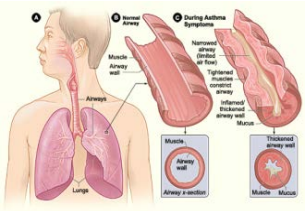
Drug

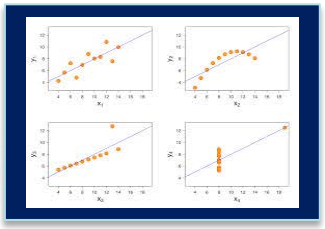


Organism



Disease





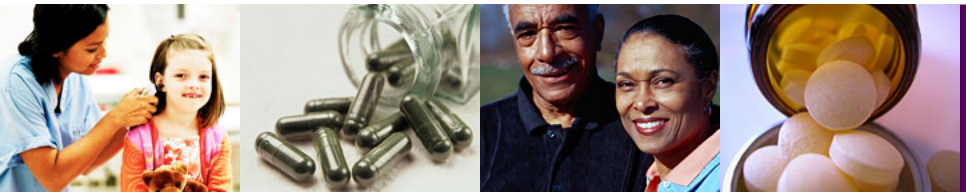
Quantitative Methods and Modeling

- Maximize what we can learn from existing data
- Bridge information gaps caused by practical or ethical difficulties that limit *in vivo* and *in vitro* studies
- Model and predict pharmacokinetics
- Predict trial outcomes and optimize clinical trial design
- Extrapolate results to new scenarios
- Being applied across the entire process of drug development




Health Canada’s Experience: Outline

- Perspective
- Pharmacometrics Working Group
- Quantitative methods in drug submissions
- Current approaches
- Future directions



Perspective

- These comments reflect my perspective coming from:
  - Smaller agency
  - Biopharmaceutics
  - Scientific review
  - Pharmacometrics Working Group




Pharmacometrics Working Group

- Therapeutic Products Directorate (TPD) and Biologic and Genetic Therapies Directorate (BGTD)
- Scientific reviewers and advisors, statisticians
- Membership representing wide range of scientific review areas
- Global assessment of how quantitative methods are being applied in drug submissions to TPD and BGTD
- Guidance on future vision




Quantitative Methods in Drug Submissions

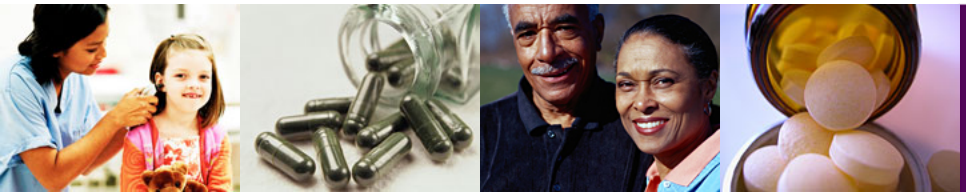
- Use of quantitative methods is submission driven:
  - Sponsors' analyses are considered case by case during drug the review process
- Number of submissions and complexity of quantitative analyses is increasing over time
  - Often in complex submissions to support more challenging decisions
- More frequent application in pivotal, rather than supportive, role




Quantitative Methods in Drug Submissions

Estimated annual average number of submissions containing pivotal or supportive pharmacometric analyses, during 2012-2015

	TPD	BGTD	Total
Clinical Trial Applications	**526**	**216**	**742**
New Drugs	**72**	**31**	**103**
Generic Drugs	**2**	**-**	**2**



Quantitative Methods in Drug Submissions

Types of applications: Examples

- Selection of doses for use in pediatric clinical trials
- Optimization of labeled dose based on target plasma concentrations
- Support for new routes of administration
- Support for new dosage forms or new fixed dose combinations
- Use and dose modification in subpopulations not tested in clinical trials (e.g., patients with moderate to several renal or hepatic impairment)
- Drug labelling for drug-drug interactions
- Generic drugs: *in vitro – in vivo* correlation modeling




Quantitative Methods in Drug Submissions

- Inclusion of modeling and simulation in generic drug submissions to Health Canada has been limited
  - Much less common than for innovative drugs
  - This limits our awareness of how sponsors may be using such approaches during generic drug development
  - More frequent inclusion of quantitative analyses in submissions for information purposes would be welcome




Current Approach

- Submission driven, case-by-case assessment
- Reviews led by diverse therapeutic areas rather than centralized process
- Consultations
  - Office of Science
  - External experts
- At this time, we are not pursuing such analyses independently (e.g., in development of bioequivalence standards)




Future Directions

- Targeted investment in in review capacity
  - Hiring pharmacometricians
  - Training clinical reviewers
- Improve strategic use of quantitative methods
  - Coordinated approach across the agency
  - Development of guidelines on conduct and reporting
  - International collaboration and harmonization
  - Expect increased and more complex use
  - Initiation of in-house analyses in future
  - Generic drugs: opportunities




Future Directions: Generic Drugs

- Optimization of data requirements to show bioequivalence or therapeutic equivalence
- Avoid studies that have poor discriminative power
- Increased reliance on the results of quantitative methods in pivotal decisions for generic drugs will depend on:
  - Demonstrated predictive value and validation
  - Accumulated experience
- Quantitative methods applied in the development of comparative bioavailability standards will need to meet high bar of reliability and consider product-specific risk




Future Directions: Generic Drugs

- Health Canada’s current regulatory review modernization efforts include focus on:
  - Improving access to generic drugs
  - International collaboration and harmonization
- Continuing discussions with international agencies on the use of quantitative methods to modernize generic drug development and review will help us reach these goals.




Pharmacometrics Working Group Members

- Ariel Arias, Centre for Biologics Evaluation, BTGD
- Alex Bliu, Centre for Evaluation of Radiopharmaceuticals and Biotherapeutics, BGTD
- Hema Gupta, Bureau of Gastroenterology, Infection, and Viral Diseases, TPD
- Baskar Mannargudi, Bureau of Metabolism, Oncology, and Reproductive Sciences, TPD
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