U.S. FOOD & DRUG ADMINISTRATION

Use of Data Analytics Approaches to Support Regulatory Assessment - from FDA Perspective

Meng Hu

Division of Quantitative Methods and Modeling (DQMM)
Office of Research and Standards
Office of Generic Drugs
CDER | U.S. FDA

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Disclaimer

- This presentation reflects the views of the author and should not be construed to represent FDA's views or policies.

Outline

- Background
- Opportunities of using data analytics approaches
- Our efforts
- Case studies
- Discussion

Background

- One critical mission of FDA is to ensures high-quality, affordable generic drugs are available to the American public.

- The FDA-published guidances provide important information on the regulatory pathway for generic drug approval.

- For some drug products, research/regulatory gaps still exist, which impede the generic drug development and regulatory assessment, such as equivalence analysis/demonstration based on complex in vitro data.

Background

- The arrival of the Big data era has brought unprecedented advances on data analytics approaches, such as
  - Multivariate (statistical) analysis
  - Model-free algorithm
  - Artificial intelligence

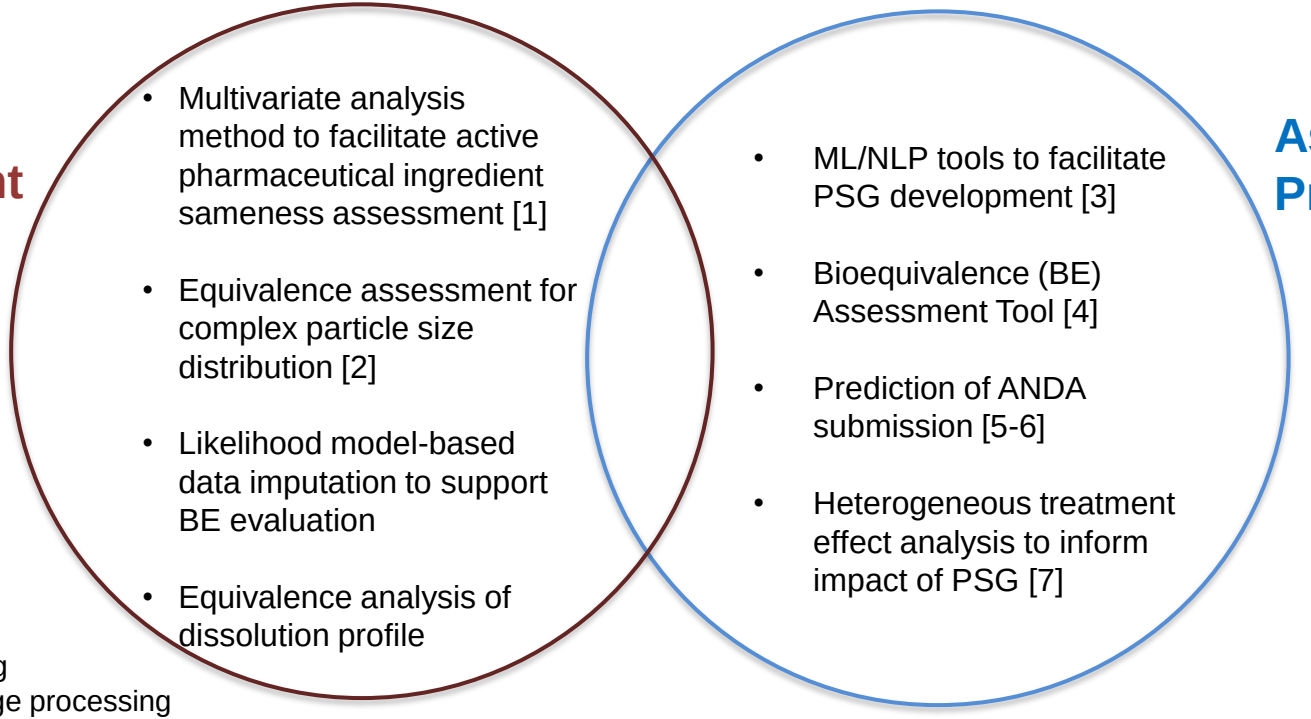
- The advancement in data analytics offers opportunities to support generic drug development and regulatory assessment.

Opportunities

- Supporting regulatory assessment
  - Complex equivalence analysis

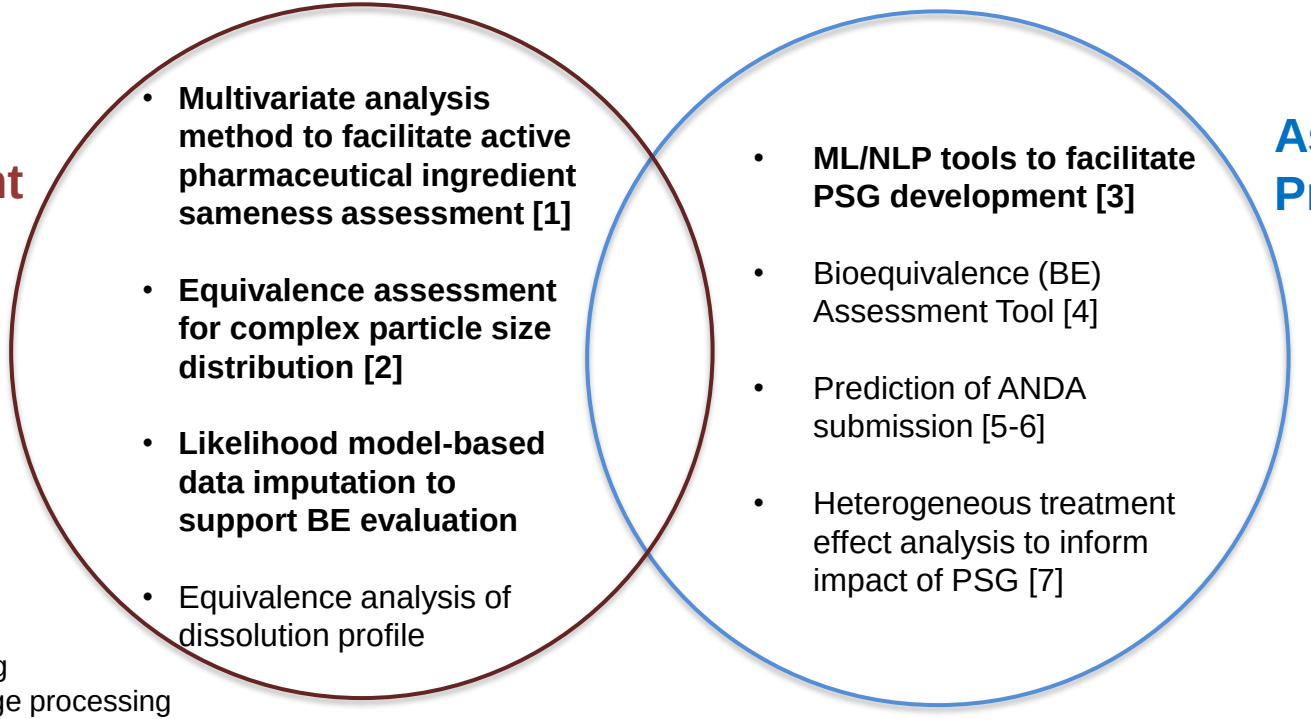
- Facilitating assessment process
  - Automation tools; Business intelligence

Regulatory science to answer the opportunity call



ML: machine learning
NLP: natural language processing
PSG: product-specific guidance
ANDA: abbreviated new drug application

Regulatory science to answer the opportunity call



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Case Studies

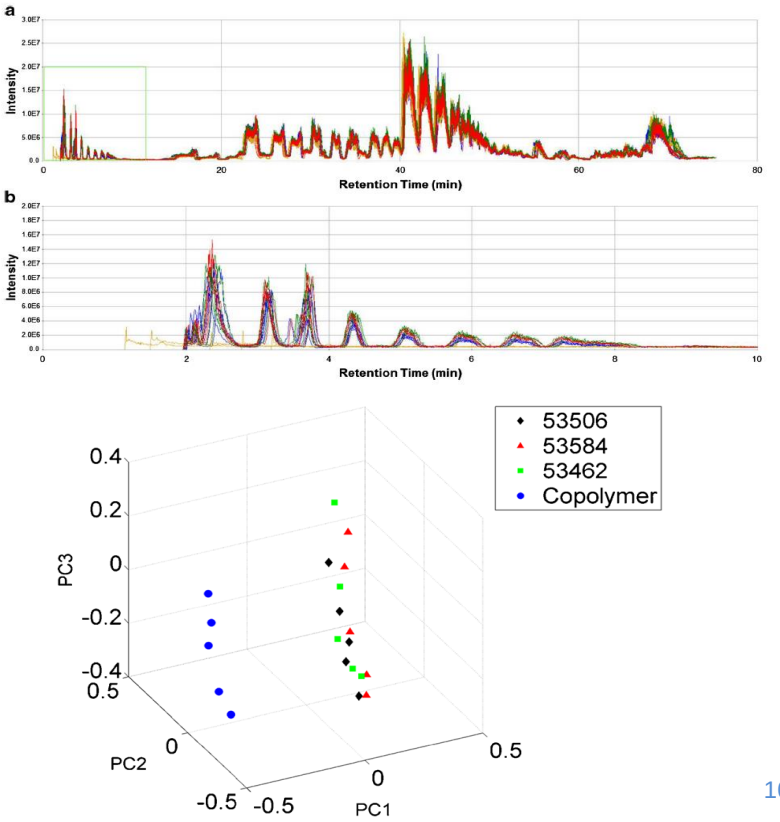
Sparse Principal Component Analysis for Glatiramer Acetate Injection BE Evaluation

Glatiramer acetate injection: used to treat relapsing-forms of multiple sclerosis (MS), including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease

Background: API sameness assessment involves Liquid chromatography–mass spectrometry (LC-MS) profiles similarity evaluation.

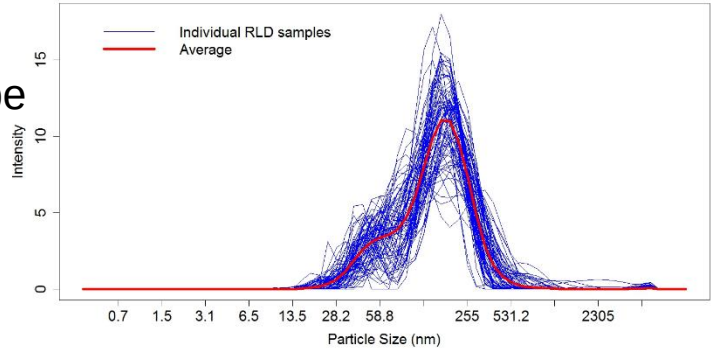
Question: How to evaluate the similarity of LC-MS profiles, which have hundreds of components?

Impact: Innovative Sparse Principal Component Analysis (SPCA) was used to reduce the dimension of data to 3 feature variables and several ANDAs were approved.



Earth Mover's Distance for Cyclosporine Ophthalmic Emulsion BE Evaluation

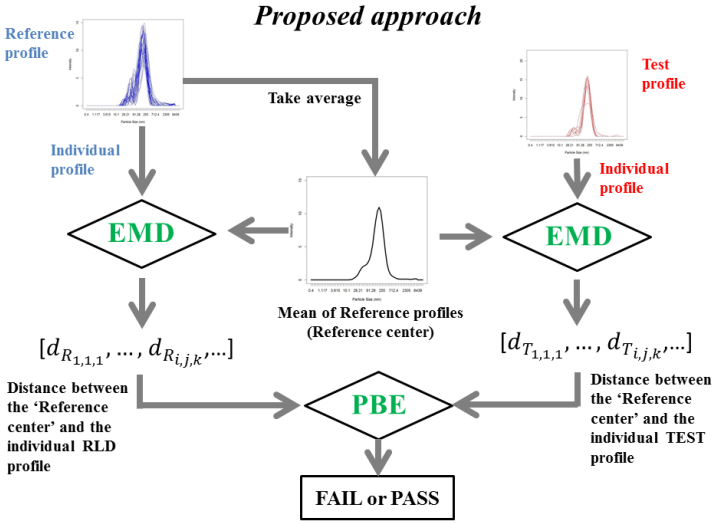
Cyclosporine Ophthalmic Emulsion: indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca .

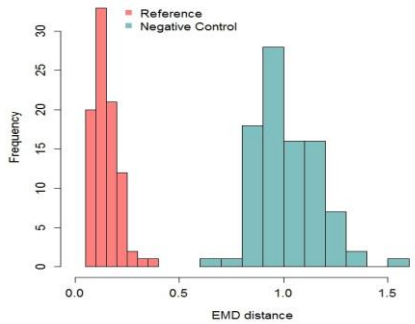


Background: PSG recommends *in vitro* approach including particle size distribution;

Question: How to assess the equivalence of complex particle size distribution (PSD) profiles (i.e., multimodal) between the test product and reference standard?

Impact: Earth Mover's Distance (EMD) Based Equivalence Approach was recommended in the PSG. An ANDA was approved.





Likelihood Model Based Data Imputation to Support BE Evaluation for Albuterol Sulfate Inhalation Aerosol

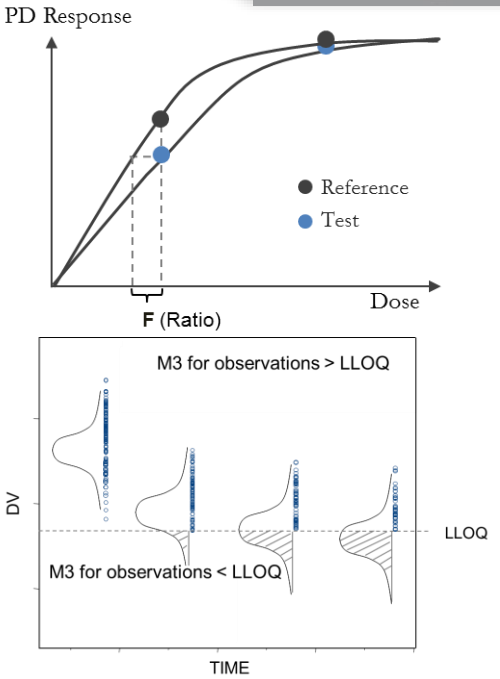
Albuterol Sulfate Inhalation Aerosol: a beta$_2$-adrenergic agonist indicated for treatment or prevention of bronchospasm in patients 4 years of age and older.

- **Public Health Emergency Designation COVID-19 Generic Drug Product**
- **First Generic Priority ANDA**

Background: PD BE bronchoprovocation study conducted by the applicant included considerable amount of censored values (out of detection limit) in PC20 data.

Question: How to assess PD BE given the high percentage of censored values in the study data?

Impact: FDA's internal analysis adopted a states-of-art likelihood-based modeling approach (M3 model) to perform data imputation for censored value. This modeling approach improves the credibility of the PD model and provided the model-integrated evidence to support the final ANDA approval as one of the first generics in 2020.

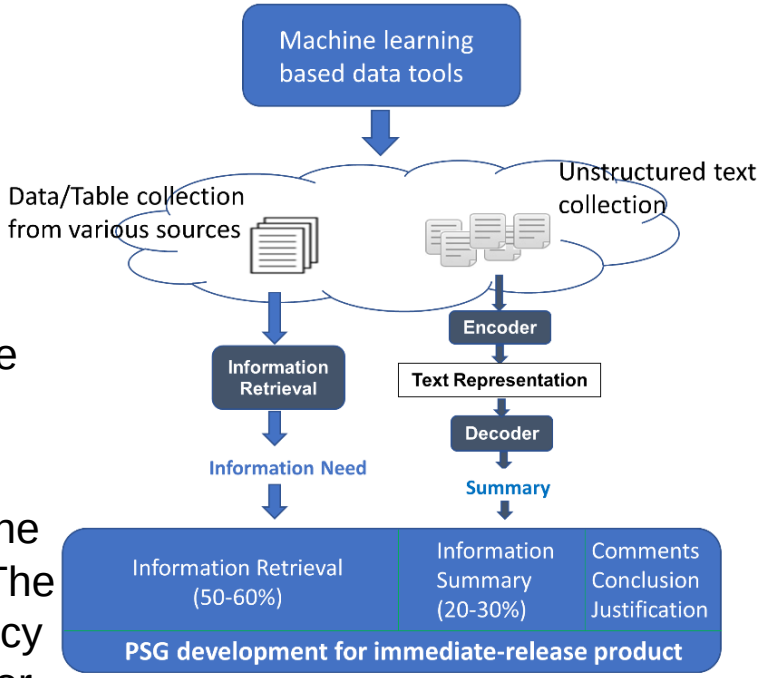


ML/NLP tools to Facilitate PSG Development

Background: PSGs represent FDA's current thinking on the optimal approaches to demonstrate BE between a test product and its corresponding reference listed drug. The time-cost analysis of PSG development process (e.g., for immediate-release product) shows that extensive efforts are needed on retrieving supportive information from the public (e.g., drug labeling) and internal (e.g., review documents) sources.

Question: Given the importance of PSG, how to facilitate the high-quality and efficient PSG development, e.g., automating labor-intensive work?

Impact: ML/NLP models were developed to streamline the information retrieval tasks during the PSG development. The developed solution enhances the efficiency and consistency of PSG development and can be potentially transferable for other information retrieval tool development .



https://www.fda.gov/drugs/generic-drugs/science-research

Summary

- Advancement of data analytics approaches bring opportunities to facilitate development and regulatory assessment of generic drugs.
  - Supporting regulatory assessment
  - Facilitating assessment process
- Please join the following panel discussion to share your thoughts/ideas.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