Scientific Approaches for the Analytical Characterization of Complex Generic Products

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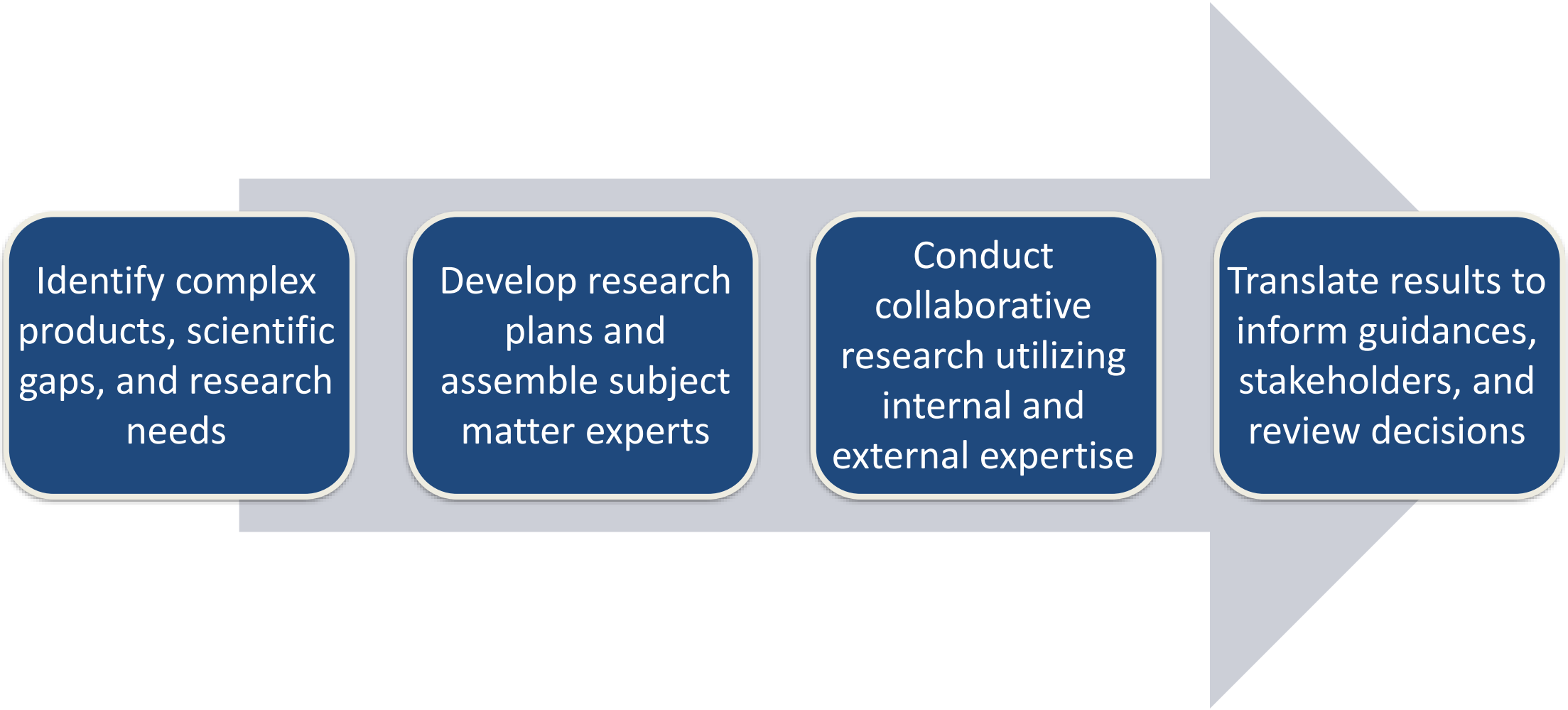
OPQ's Proactive Science and Research Approach

- The **science program** is designed to maintain preparedness
  - Consumer complaints
  - Public health issues
- The **research program** is "forward looking"
  - New and emerging technologies for analytics and manufacturing
  - Advanced analytics (instrument and modelling)
  - Forecasting generics for newly-approved NDAs
  - Complex drugs in NME and generic drugs

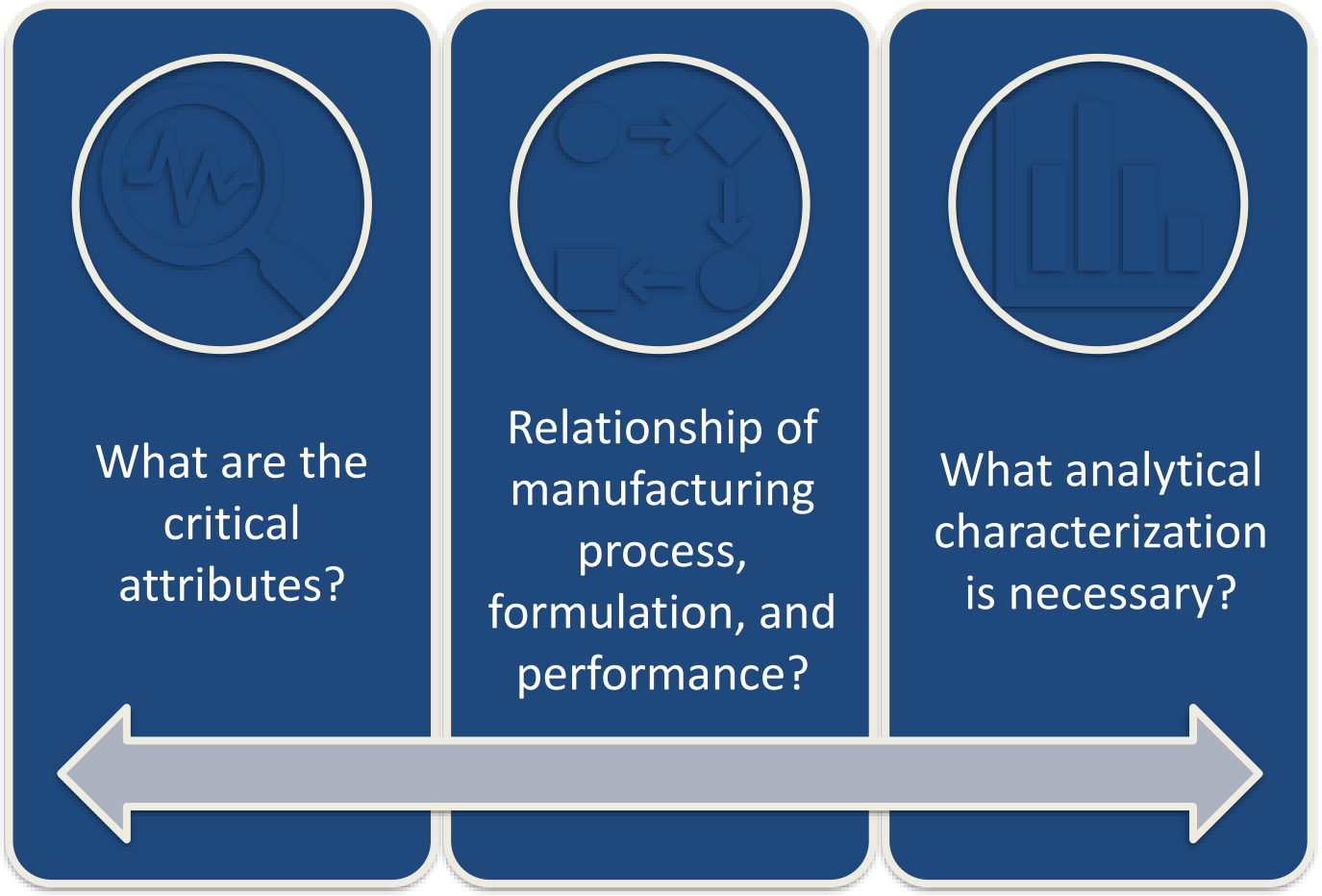
OPQ & OGD: GDUFA Research Collaborations



Analytical Characterization in Generic Drug Science

Analytical Characterization:
in Development, Manufacturing, and Post-Market evaluation

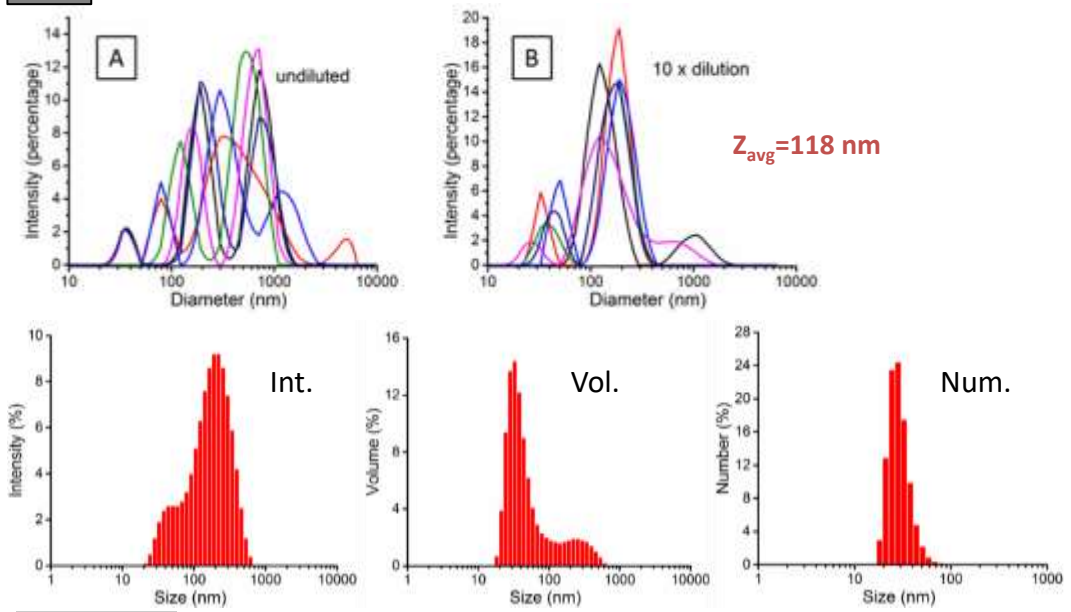
- reverse engineering
- demonstrating in vitro sameness
- BE determination
- Pharmaceutical equivalence
  - impurities identification
  - impurities quantitation
- quality control
- surveillance



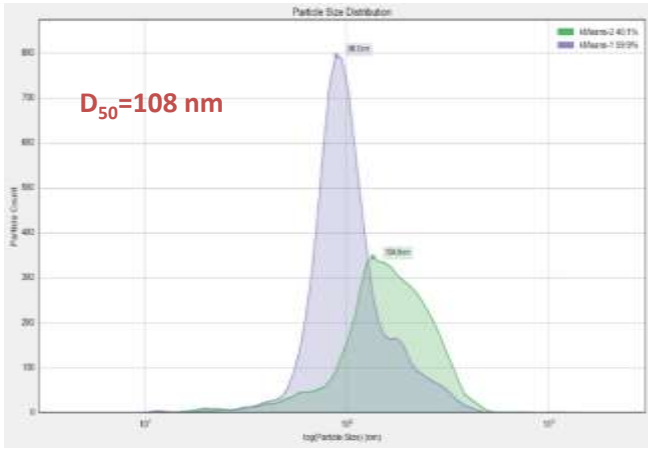
Characterization Challenge in Complex Product: Particle Size Distribution in Cyclosporine Emulsion

- manufacturing techniques can manipulate PSD
- particle size likely affects drug distribution
- particle size may impact overall drug release

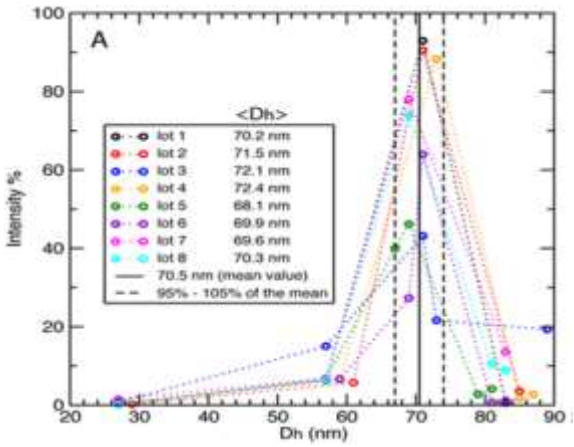
DLS



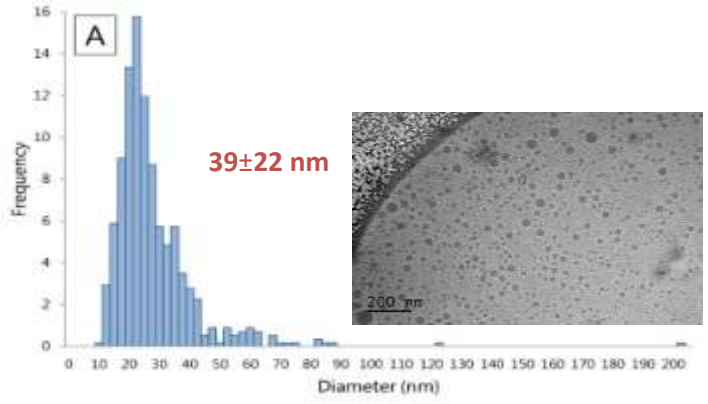
NTA



DOSY NMR



Cryo-TEM



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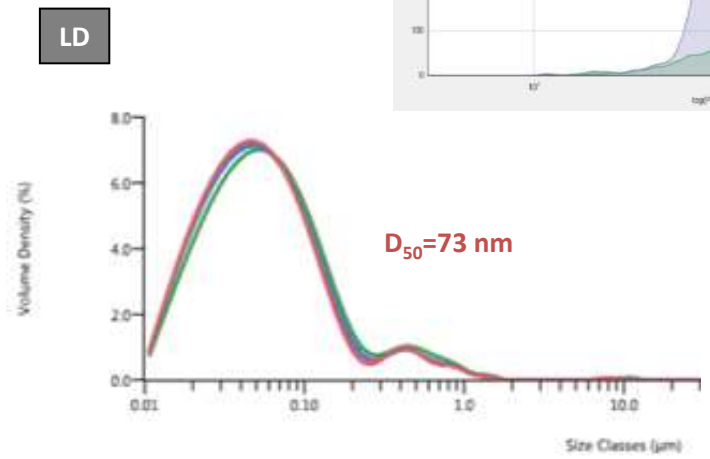
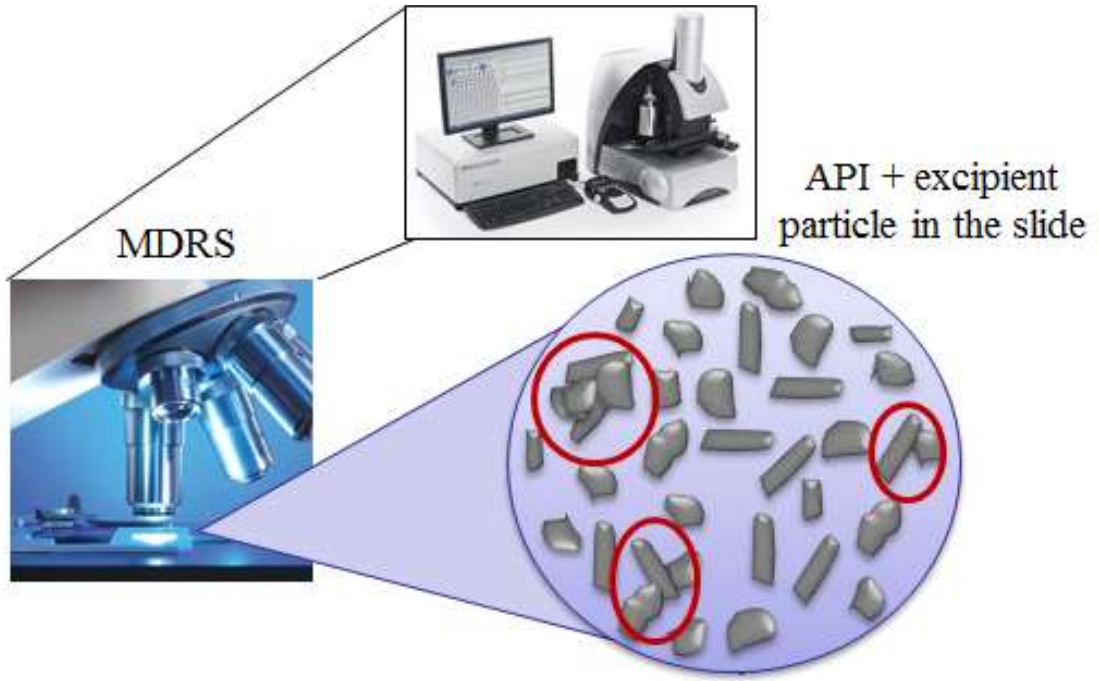


P. Petrochenko, N. Pavurala, Y. Wu, S. Y Wong, H. Parhiz, K. Chen, S.M. Patil, H. Qu, P. Buoniconti, A. Mohammad, S. Choi, D. Kozak, M. Ashraf, C.N. Cruz, J. Zheng, X. Xu. Analytical Considerations for Measuring the Globule Size Distribution of Cyclosporine Ophthalmic Emulsions. International Journal of Pharmaceutics (2018). 550(1-2), 229-239

Impacts of GDUFA-Funded Research

- alternative approaches to characterize generic nasal suspension drug products

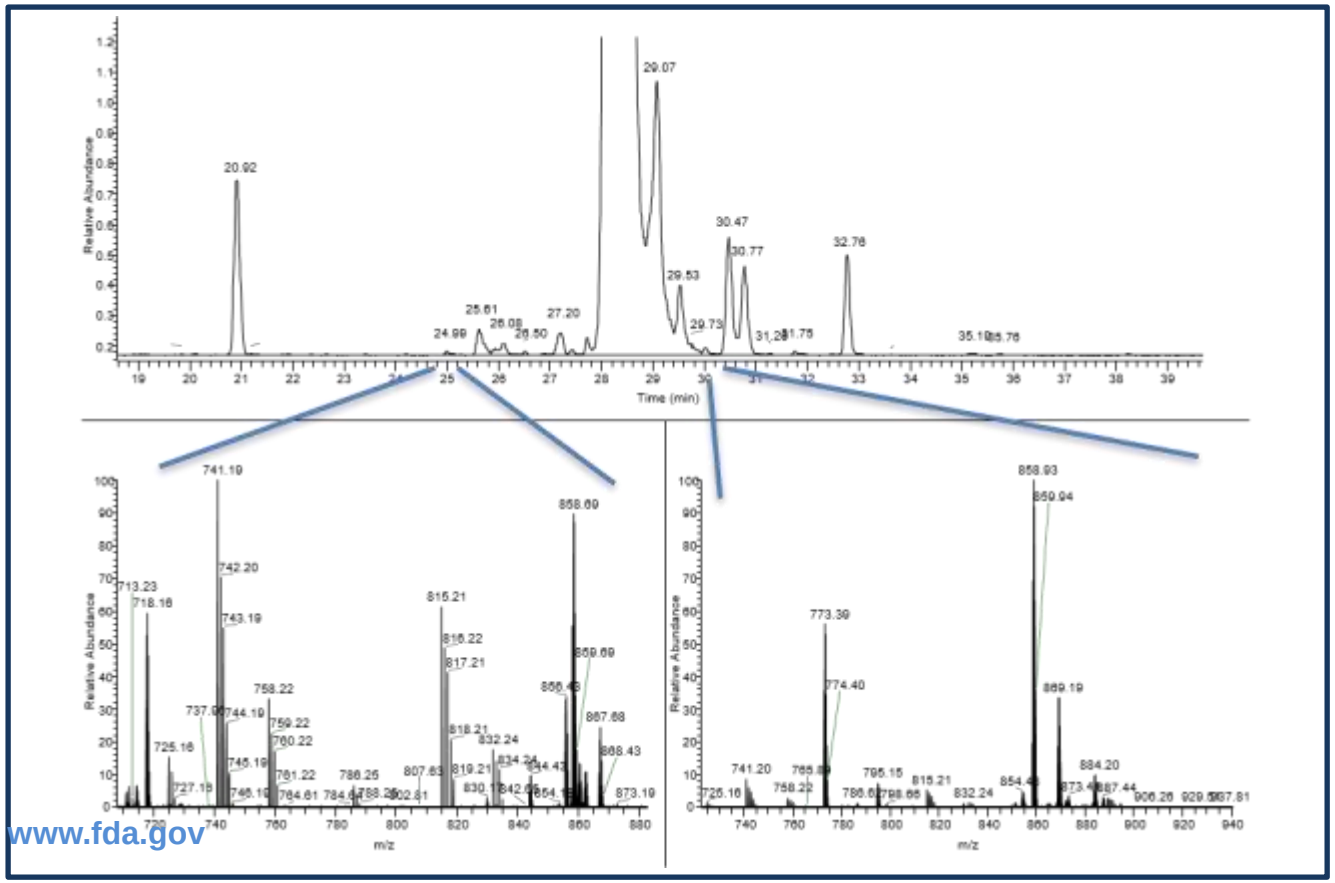


Morphology-Directed Raman Spectroscopy

(1) Q. Liu, M. Absar, B. Saluja, C. Guo, B. Chowdhury, R. Lionberger, D. Conner, B. Li, Scientific Considerations for the Review and Approval of First Generic Mometasone Furoate Nasal Suspension Spray in the United States from the Bioequivalence Perspective, *The APPS Journal*, 2019.
(2) B. Thomas, M. Absar, R. Devadia, D. Conti, K. Witzmann, C. Guo, Analytical Method Development for Characterizing Ingredient-Specific Particle Size Distributions of Nasal Spray Suspension Products, *J. Pharm. Sci.*, accepted.

Impacts of GDUFA-Funded Research

- alternative approaches to characterize generic nasal suspension drug products
- development of workflows for impurity analysis in therapeutic peptide products



Liquid Chromatography with High Resolution Mass Spectrometry

ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/andas-certain-highly-purified-synthetic-peptide-drug-products-refer-listed-drugs-rdna-origin

Impacts of GDUFA-Funded Research

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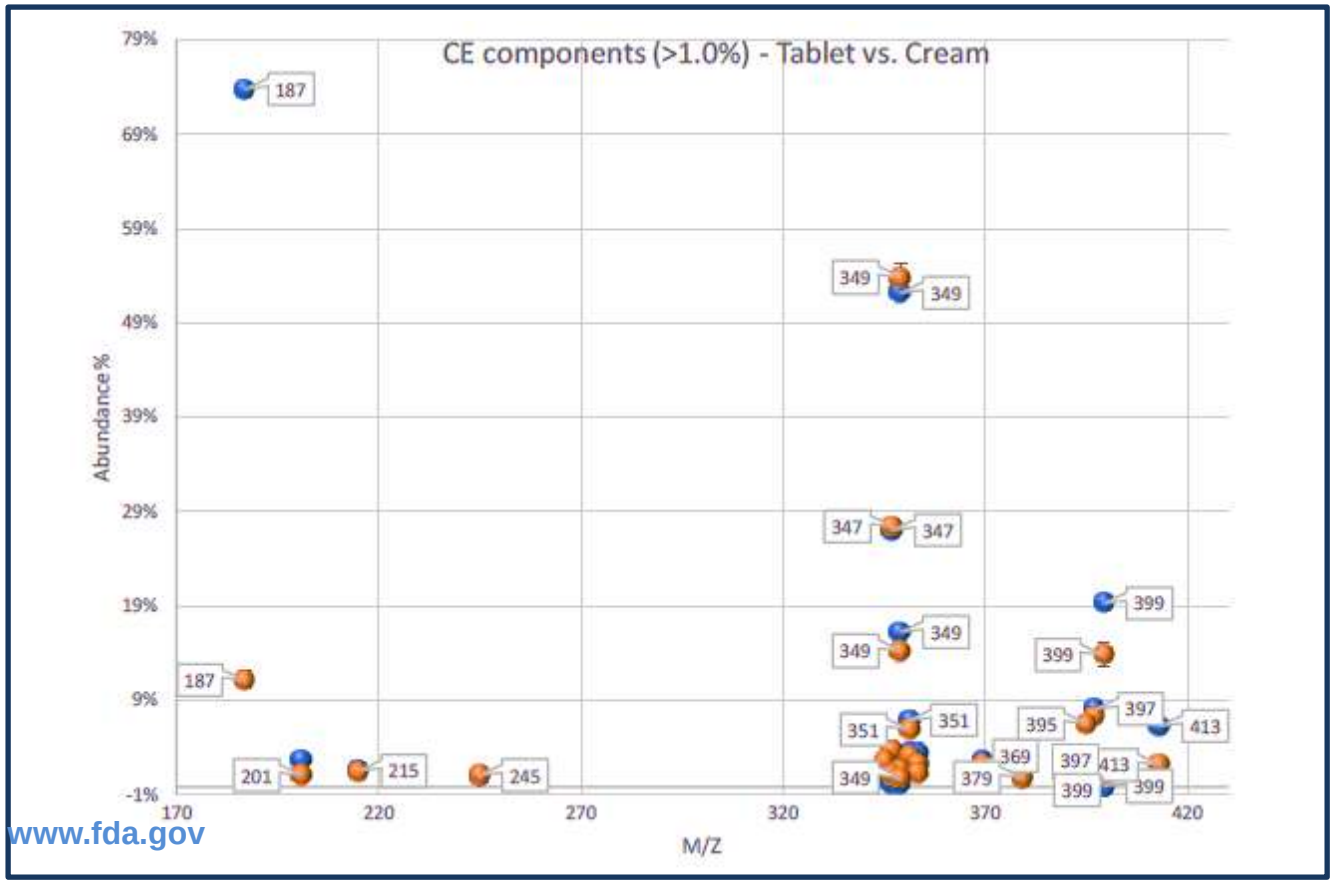
- development of workflows for impurity analysis in therapeutic peptide products
- method development to demonstrate API sameness

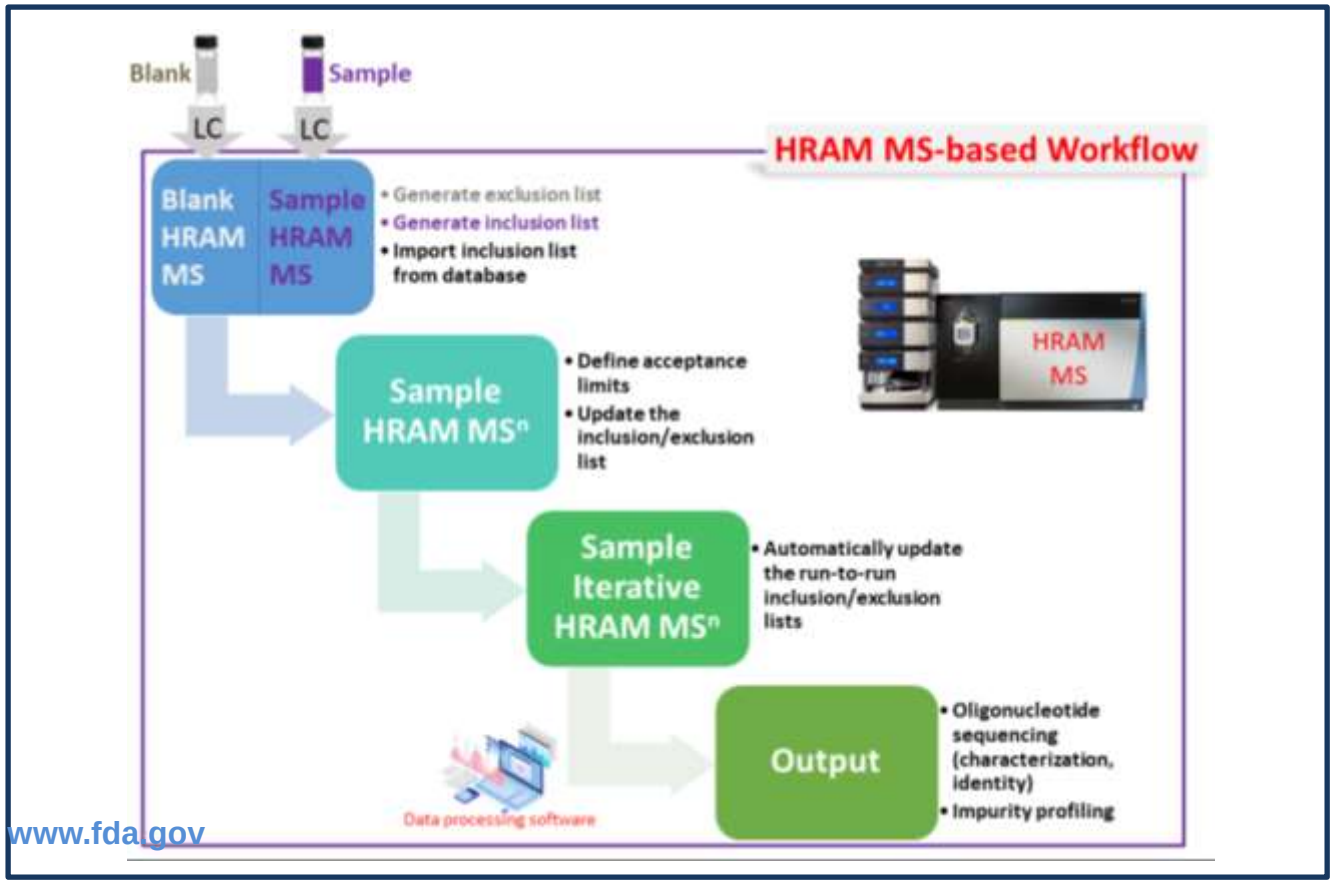


Ultra High-Performance Liquid Chromatography with Mass Spectrometry

Draft Guidance on Conjugated Estrogens, 2014: https://www.accessdata.fda.gov/drugsatfda_docs/psg/Conjugated_estrogens_004782_RC12-14.pdf

Impacts of GDUFA-Funded Research

- alternative approaches to characterize generic nasal suspension drug products
- development of workflows for impurity analysis in therapeutic peptide products
- method development to demonstrate API sameness
- develop methods for characterization, quality control, and stability testing of new products



High Resolution Accurate Mass Mass Spectrometry

Afternoon Break-Out Session #2
Sub-Session 1

Gaps in Complex Product Analysis

Exploring the gaps that industry and others see in the realm of complex generic product characterization, and

Discussing the types of products that should have **more focus**

Afternoon Break-Out Session #2
Sub-Session 2

New Analytical Methods and Technologies for Complex Product Analysis

Discussing **new analytical methods** that are promising for generic drug development, screening, quality control

Considering consider **access and availability** by industry, cost, and acceptance,

Identifying what plans or considerations need to be put in place to **encourage adoption of new technologies** by the generic drug industry

Afternoon Break-Out Session #2
Sub-Session 3

Assessing Current Analytical Methods and Further Development

Assessing analytical methods currently considered to be most useful and what can be done to **better develop** these technologies

Discussing the rationale for sampling and assessing batch-to-batch variability for various types of complex products