



**Your Generics & Biosimilars Industry**

# Inhalation Drug Products

**FDA Regulatory Science Workshop  
Association for Accessible Medicines  
May 24, 2018**

# Overview

- ☐ Recent Activities/Meetings for OINDPs
- ☐ Brief Outcomes from these meetings
- ☐ Recommendations for Future Activities

# Recent Activities/Meetings for OINDPs-1

FDA sponsored/participated in several conferences on understanding in vitro dissolution methods with a view to understanding potential impact on PK and PD

- [New Insights for Product Development and Bioequivalence Assessments of Generic Orally Inhaled and Nasal Drug Products—Jan 2018](#)
  - Predictive Dissolution Methods for OINDPs
  - Novel Analytical Tools for Characterization of Nasal Suspensions
  - Realistic Models for Predicting of Regional Drug Deposition
  - Computational Models to Understand In Vivo Models
  - Future Direction of Generic OINDP Regulatory Science Research

Relevance of in vitro dissolution methods and deposition studies and their impact on PK, PD  
Key Challenges to in vitro only BE pathway for Nasal suspensions and orally inhaled products

# Recent Activities/Meetings for OINDPs-2

## [IFPAC Conference Symposium- Considerations in the Establishment of Clinically Relevant Drug Product Specifications for Orally Inhaled Drug Products-Feb 2018](#)

- Considerations in the Establishment of Clinically Relevant Drug Product Specifications for Orally Inhaled Drug Products
- Critical Attributes of Orally Inhaled Products – Link Between In Vitro Properties and Therapeutic Performance
- Extending MAM/PBPK modeling approaches to help establish inhaled product specifications
- Working Towards Real Time Assurance of Clinical Performance: Formulating for PAT and Leveraging IVIVC Capabilities

Assessment of in vitro methods, PK, modelling, development of IVIVC and their predictions on PD

# Recent Activities/Meetings for OINDPs-3

## [Respiratory Drug Delivery April 24<sup>th</sup> 2018](#)

Expanding the Marketplace for Generic Inhalers via Improved Testing & Regulatory Guidance

- **New Tools for Generic Orally Inhaled Drug Products to Maximize Prospects of Food and Drug Administration Approval**
- Robert Lionberger, Ph.D., Food and Drug Administration, Silver Spring, Maryland
  
- **The Role of Comparative Analyses for Evaluation of Generic Drug-Device Combinations in an Abbreviated New Drug Application**
- Kimberly Witzmann, M.D., Food and Drug Administration, Silver Spring, Maryland

# Recent Activities/Meetings for OINDPs-3

[Respiratory Drug Delivery April 24<sup>th</sup> 2018](#)

Expanding the Marketplace for Generic Inhalers via Improved Testing & Regulatory Guidance

**Panel Discussion: Expanding the Generic Marketplace via Improved Testing Protocols and Regulatory Guidance**

**Chairman:**

**Peter R. Byron, Ph.D.**

**Panel:**

**Renish Delvadia, Food and Drug Administration**

**Sanjeeva Dissanayake, Certior Consulting**

**Robert Lionberger, Food and Drug Administration**

**Robert Price, University of Bath**

**Dennis Sandell, S5 Consulting**

**Stephen W. Stein, 3M Drug Delivery Systems**

**Kimberly Witzmann, Food and Drug Administration**

# Brief Outcomes from these meetings

## Complex Respiratory – In vitro demonstrations of equivalence instead of Clinical studies

- **Points to address (1)**

- There are many possible product attributes that can be measured, by a variety of techniques, to show in vitro properties.
  - For example, particle size, shape, adhesive properties, dissolution rate, aerodynamic particle size, emitted dose, powder flow, amorphous content, etc.
- Some of these properties can/could be shown to have a link to in vivo performance. Others are perhaps easily measured, but there is only a speculative performance link, not supported by published evidence.
  - A situation like biosimilars where there are many comparisons needed on many chemical and physical attributes to substantiate equivalence, even where there is little evidence of a link from some of these to in vivo properties may not be ideal.

# Brief Outcomes from these meetings

## Complex Respiratory – In vitro demonstrations of equivalence instead of Clinical studies

- **Points to address (2)**

- **The most desirable area to address is elimination of the clinical endpoint bioequivalence studies –** typically several hundred to over one thousand patients
- Clinically relevant in vitro tests could be developed and validated to support this
  - These may differ according to the therapeutic class of the active ingredient (e.g. depending on the site of action, or the expected pharmacodynamic response)

-OR-

- The physical-chemical properties of the active ingredient (for example solubility, absorption properties)



# Recommendations for Future Activities

- ❑ We hope the Agency continues to sponsor programs that enhances a deeper understanding of the impact of Critical Material Attributes, Critical Process Parameters and Analytical Procedures on clinically relevant parameters.
- ❑ FDA science should aim to narrow down the plurality of potential equivalence attribute comparisons to those **having a clear link to in vivo performance**. In particular, comparisons to show IVBE should be readily measurable by widely available techniques where the validity has been established by (for example) peer reviewed publications, or acceptance as pharmacopeial methods.
- ❑ FDA science should also ensure that statistical methods and acceptance criteria required to make comparisons are demonstrated to be relevant and appropriate to the equivalence attribute being tested.

## Guidances

- ❑ Publish results from sponsored studies and update guidances.

