

# **European Pharmacopeia Perspectives on Efficient Data Analysis (EDA) and Abbreviated Impactor Measurement (AIM)**

S C Nichols  
OINDP Consultant

steven.nichols3@btinternet.com

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## **Items to be Covered**

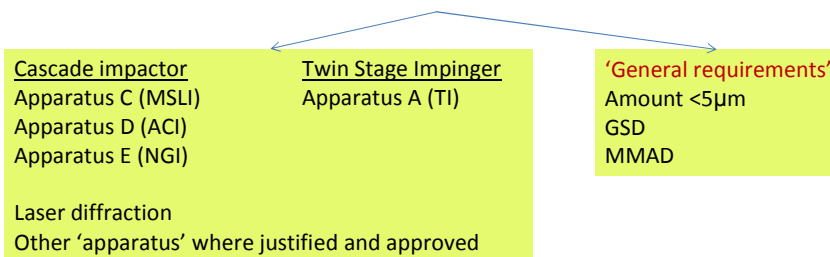
- Current Pharmacopeia Requirements
- Introduction to EDA and AIM
- Why include AIM and EDA in Ph. Eur.?
- Ph. Eur. Test Requirements and Process
- AIM Apparatus and Evidence
- Efficient Data Analysis (EDA) and Specifications
- Conclusion

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## Current Ph. Eur. Requirements

- European Union directives 2001/82/EC, 2001/83/EC and 2003/63/EC (amended), on medicines for human and for veterinary use, maintain the mandatory character of European Pharmacopoeia specifications on medicines for marketing authorization applications for OIPs

- Inhalation Methodology and Requirements



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## Current Ph. Eur. Requirements

– Target of current methods is restricted to:

- Respirable mass <math><5\mu\text{m}</math>
- Aerosol characteristics (MMAD, GSD)
- Small sample size, Little data analysis, No relationship to manufacturing Capability (pass:failure rate)
- Does not provide any scientific correlation to *in vivo* data

– Ph. Eur. Purpose

- Commercial batch quality
- Drug Product quality assessment tool
- Comparator method to batches used in pivotal clinical trials?
- Concept of alternate analytical methods in Ph. Eur. General Notices (1)

– The EMA guideline on inhalation and nasal products

- Allows alternative procedures as long as validated analytical methods are used

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## Introduction to AIM-EDA

1. EDA-AIM is proposed as an **alternate approach** for product quality assessment.
2. Not a replacement to current Compendial requirements.
3. EDA application is primarily on Quality Control.
  - An improved approach with two separate and independent metrics.
  - ISM, LPM:SPM ratio
4. AIM – the tool by which to acquire the metrics.

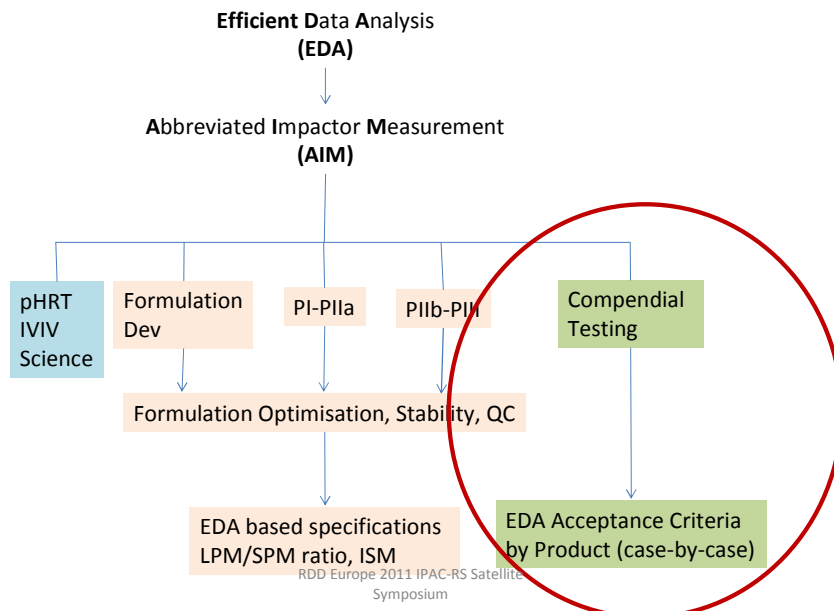
### Refs:

Tougas et al. AAPS PharmSciTechnol., 2009; 10(4): 1276-1285

Mitchell et al. AAPS PharmSciTechnol., 2010; 11(2) 843-851

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## Introduction to AIM-EDA

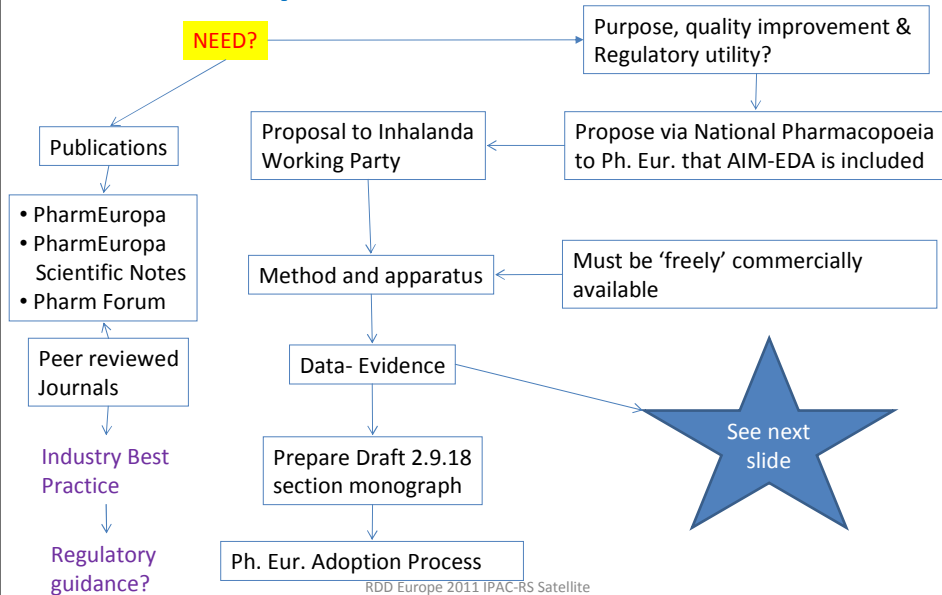


## Why include AIM and EDA in Ph. Eur.?

- Will establish a legal position for AIM & EDA
  - Thus, voiding the need for demonstration of equivalence to Pharmacopoeial method in MAAs.
- Harmonised Methodology
  - Within EU, US & ROW
- Aids consistent data between Industry and
  - Approval agencies
  - Notifiable bodies
- An 'industry' identified need
  - Much more efficient
  - Quality assurance improvements
- 'Scientific' need
  - Enhanced data analysis - more meaningful
  - Potential IVIV applications

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## Requirements and Process



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## Requirements and Process - DATA

- Evidence (FIT FOR PURPOSE)
  - Application to OINDPs
    - As broad as possible to DPIs, MDIs, Aqueous & Nebulisers
    - ‘Useful’ cut-points
      - how do we deal with current 5µm requirement?
  - ‘Quality’ Benefit
    - Over and above that currently available from existing apparatuses and data analysis
    - Ability to distinguish ‘good’ vs. ‘OOS’ batches
  - Impactor Calibration Data (Published)
    - Collection efficiency curves
    - Cut-points
    - Flow rate data – available options covered or correction factors

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## AIM Apparatus and Evidence

Apparatus	Calibration Data	Products Tested	Flow Rates	Publications
Copley fast screening Andersen (FSA)	Mono-dispersed particles @ several flows	DPI, pMDI	28.3-90 l/min	DDL 21 AIM workshop* & AAAPSP Pharm SciTech
MSP fast screening impactor (FSI)	Mono-dispersed particles @ range of flow rates	DPI, pMDI, nebulisers	15-100 l/min	DDL 21 AIM workshop*
Westech fine particle dose Impactor (FPDI)	Dynamically calibrated @ range of flow rates	DPI, pMDI	15-100 l/min	Due 2011



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Available at [www.EPAG.co.uk](http://www.EPAG.co.uk) – public documents folder

## AIM Apparatus and Evidence - Issues

- **Potential for many apparatus options!**
  - Which one(s) would be specified in the Ph. Eur.?
    - Already ACI modifications used routinely (non-Ph. Eur.)
      - Modified stages (-1, -2) & 'standard' ACI at 60L/min
    - Industry would have to advocate
    - Would still require a general clause
      - 'where approved and justified'
- **Cut point selection**
- **Standards**
- **Data analysis**
  - Would not require EDA unless sample size increased
  - Why would this be needed?
    - Only if current Ph.Eur. procedure is not deemed robust enough to be able to assess product quality?

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## Efficient Data Analysis (EDA) and Specifications

- **Capability of EDA to provide improved sensitivity to small changes in APSD compared with stage grouping**
    - Leading to better decision making with respect to batch disposition in the QC environment
  - **Applicability throughout the life-cycle of the OIP**
    - Innovator vs. Generic issues – specifications!
  - **Specifications**
    - General requirements (as now)
    - New 'General' requirements based on EDA metrics?
- OR**
- Would it be appropriate to have product specific specifications for APSD gathered using AIM apparatus

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## Conclusion I

- **Potentially beneficial for both Regulators and Industry to include AIM in to the Ph.Eur.**
  - But not absolutely necessary
  - Smoother path of acceptance in dossiers
  - Harmonised product testing - assessment
- **AIM is an alternative approach that should secure the same quality of data with less effort**
  - If true, then EDA metrics would not be required
- **Are the following areas satisfied?**

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## Conclusion II

- **Are the Quality benefits established?**
  - **Applicable to a range of OINDPs?**
    - & in common practice
  - **Apparatus available & 'Fit for Purpose'?**
    - Calibration data published
    - Harmonised methodology possible
    - Understanding AIM data wrt 'Full' cascade impactor
    - Validated methodology
  - **AIM in peer reviewed publications?**
    - Draft monograph for assessment
  - **Regulatory agency acceptance?**
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- **These areas must be filled before accepted by Ph. Eur.**

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