

IPAC-RS Model OINDP Initiative

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Overview

- Background
- OINDP Perspective on New Initiatives
- OINDP-specific P2 framework
- Next Steps

Model OINDP Working Group

■ Objectives

- To consider how new regulatory initiatives such as Quality by Design may be applied to OINDP
- To provide tools for use by OINDP industry in implementing new initiatives
- To engage regulators in dialogue over application of new initiatives to OINDP

Can QbD be applied to OINDP?

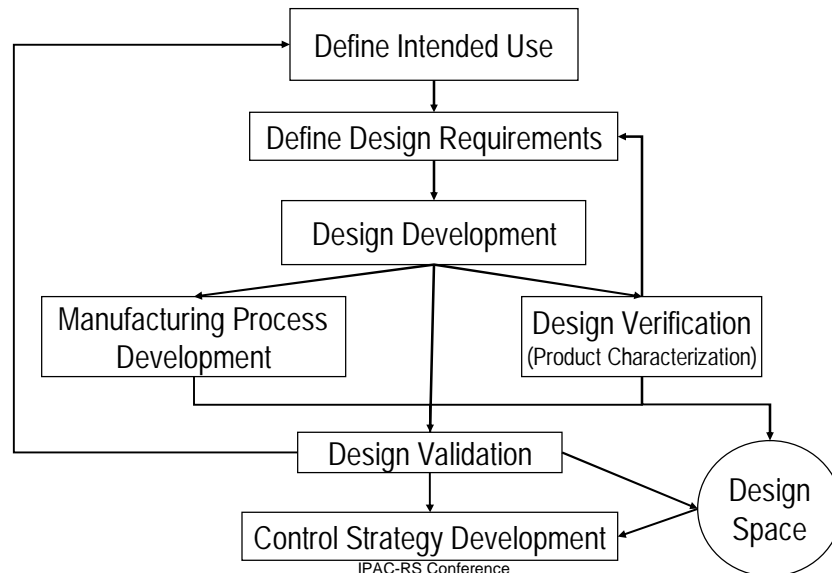
- Main difference between OINDP and other dosage forms is the level of complexity, e.g.,
 - Container Closure System
 - Particle Size Distribution
 - Interaction between formulation, container closure system, and device
- QbD is equally applicable to OINDP provided these complexities are accounted for
- OINDP may have head start:
 - QbD concepts have been used for device development
 - This information was not typically filed

What does QbD look like for OINDP?

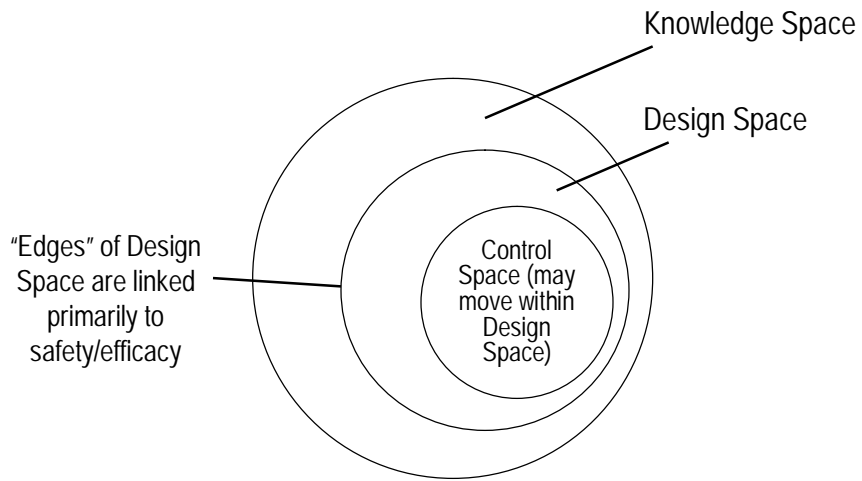
- For OINDP, many different container closure and device components interact with each other and the formulation. This may impact
 - Design requirements (may be trade-offs between requirements for different components)
 - Design spaces
 - Manufacturing processes
 - Control strategies

Pharmaceutical Development "Desired State"

Based on Device Design Concepts



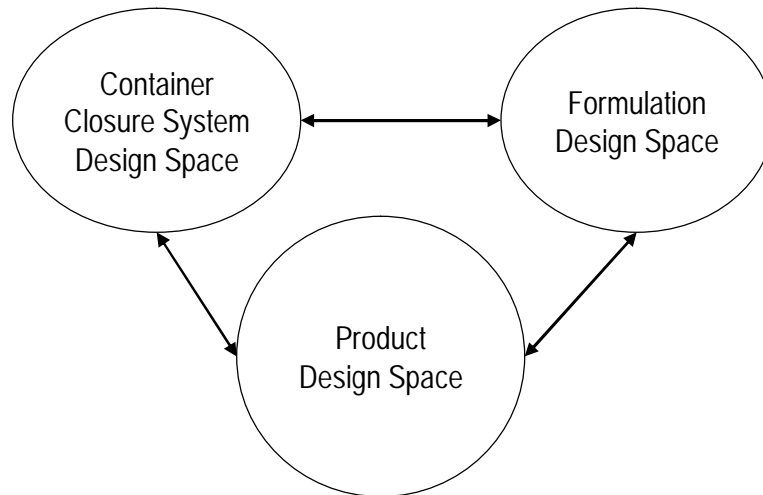
Design Space Refresher



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Some OINDP-Specific Considerations: Multiple Design Spaces Interacting



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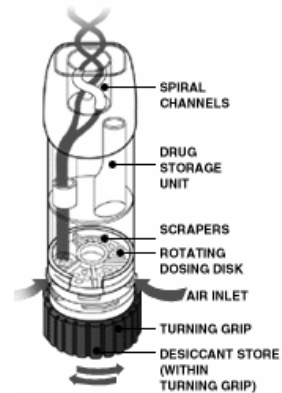
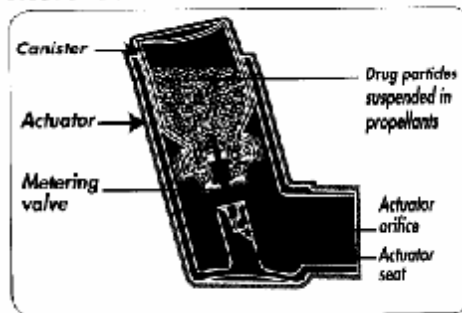
Some OINDP-Specific Considerations: Multiple Design Spaces Interacting

■ Example:

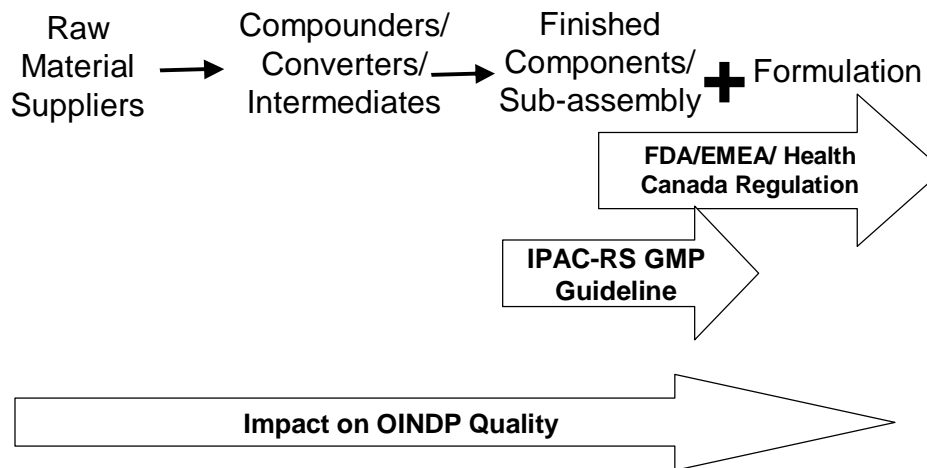
- Formulation interacts with delivery device components to produce particle size distribution of OINDP
- Particle size distribution has implications for product efficacy

Some OINDP-Specific Considerations: Multiple Components & Materials

Metered Dose Inhaler



Some OINDP-Specific Considerations: Control of Multiple Components & Materials



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OINDP-Specific Tool for Implementing QbD: P2 Framework

- Taking into account OINDP-specific considerations, WG is developing guidance on content of P2 for an OINDP
- 3.2.P.2 Pharmaceutical Development
 - “Provides an opportunity to present the knowledge gained through the application of scientific approaches and quality risk management to the development of a product and its manufacturing process”
 - “Demonstration of greater understanding of pharmaceutical and manufacturing sciences can create a basis for flexible regulatory approaches”

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OINDP-specific P2 Framework

- Intended as tool for sponsors writing a P2 for an OINDP; describes in general terms what to include
- Supplements guidance in ICH Q8

OINDP-specific P2 Framework

- Works within existing ICH guidance for P2
 - No major sections have been added, only sub-headings
 - Q8 guidance is referenced for most sections
 - IPAC-RS guidance is added only where necessary to address issues important to OINDP that are not covered in Q8, e.g., more detail in container closure section

OINDP-specific P2 Framework

■ General Considerations

- Prior knowledge
 - § Especially helpful for OINDP because of delivery platforms/systems
 - § Should be described where relevant
- Risk analysis and management
 - § Especially helpful for OINDP in order to assess large number of interacting factors (formulation, container closure system components, device components, etc)

OINDP-Specific Considerations: Physiochemical and Biological Properties

- ### ■ Particle size of the product and of the drug substance
- Influence of APSD on product performance
 - Clinical relevance of particle size
 - § Relationship between particle size and deposition
 - § Relationship to PK/PD and/or bioavailability
 - § Particle sizes studied in clinic
 - Justification for particle size in commercial product

OINDP-Specific Considerations: Container Closure System (CCS)

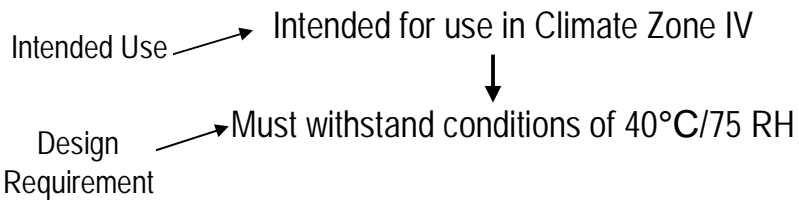
- Also includes any distinct delivery device
- Description
 - Component Selection
 - § Composition
 - § COAs
- Intended Use
 - Based on product profile
 - Considers
 - § User needs and risks
 - § Formulation requirements
 - § Environmental conditions for use
 - § Potential misuse
 - § How these are addressed

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OINDP-Specific Considerations: Container Closure System (CCS)

- Design Requirements
 - Translate Intended Use into Qualitative/Quantitative design statements
 - E.g:



- Consider:
 - § Compatibility with Formulation
 - § Material Performance
 - § L&E

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OINDP-Specific Considerations: Container Closure System (CCS)

■ Design Development

- Describes the translation of the design requirements into a container closure system/device design that meets those requirements
- Design Process
- Manufacturing Process
 - § Changes made during scale-up (e.g., single cavity to multi-cavity molds)
 - § Equivalence of components from small-scale versus industrial scale process
 - § Interaction between formulation and CCS manufacturing processes
 - § Ability to manufacture within design space

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OINDP-Specific Considerations: Container Closure System (CCS)

■ Design Development cont'd

- Design Verification
 - § Demonstrates that design requirements are fulfilled
 - § Describes approach, rationale, results
 - § L&E
 - Summary of L&E Studies
 - Approach and use of safety thresholds
 - Extraction studies; major extractables
 - Leachables studies; major leachables
 - Correlation between leachables and extractables
 - Routine Control
 - § Product Characterization
 - In order to fully characterize CCS, must perform product characterization studies on product
 - Discusses selection and use of applicable drug product characterization studies

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OINDP-Specific Considerations: Container Closure System (CCS)

■ Design Space Definition

- Describes design spaces of CCS and device
 - § Derived from design verification and validation and from formulation development
- Interactions and interdependence between formulation, CCS, and device design space

■ Design Validation

- Describes product performance (e.g., in user or clinical studies) to demonstrate that intended use has been achieved
- Describes relationship of design spaces to clinical performance
 - § Identifies COAs and links them to safety or efficacy

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OINDP-Specific Considerations: Container Closure System (CCS)

■ Control Strategy Rationale

- Based on design space
- Describes selection of tests
 - § online testing/PAT
 - § end product testing
- Describes opportunities for regulatory flexibility, e.g:

APSD linked to efficacy \Rightarrow CQA



APSD correlated to orifice dimensions



Control APSD by controlling orifice dimensions (rather than via

CI)

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Next Steps

- Complete mature draft of OINDP-specific P2 framework
- Obtain feedback from/open dialogue with
 - Industry
 - Regulators

Model OINDP Working Group Members

Jackie Schumacher, Pfizer (CO-CHAIR)

Liuda Shtohryn, AstraZeneca (CO-CHAIR)

Jeff Blumenstein, Pfizer

Claire D'Abreu-Hayling, Sanofi-Aventis

Michael Golden, GlaxoSmithKline

Laurence Huxham, AstraZeneca

Stefan Leiner, Boehringer Ingelheim

Terry Tougas, Boehringer Ingelheim