



## Overview of OINDP—Extractables, Related Issues and Challenges

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IPAC-RS Symposium:

Extractables in Materials for Inhalation & Nasal Drug Products  
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## IPAC-RS OINDP Materials Working Group

Previously known as IPAC-RS Elastomers Working Group



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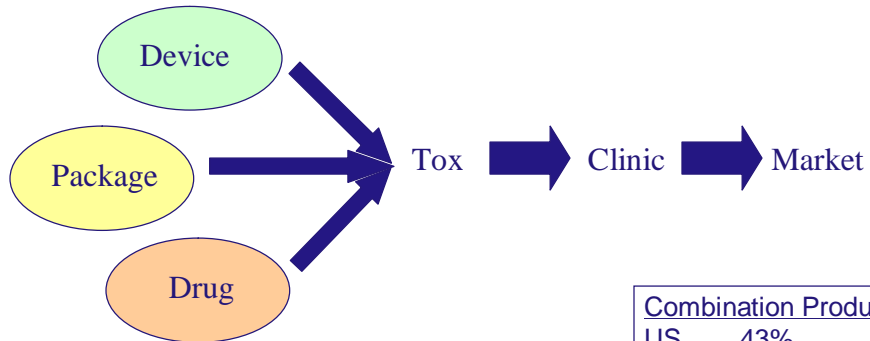


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## OINDP Overview



### Modes of Administration

- Oral Inhalation
- Nasal

### Combination Products

US	43%
EU	30%
Japan	11%
Others	16%

OINDP = Orally Inhaled and Nasal Drug Products

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## Inhalation Device Overview

### Compressed Air Based Nebulizers

#### Dry Powder Inhalers (DPIs)

- Breath synchronized nebulizers
- Compressed gas generation
- Numerous patient driven DPIs

### Liquified Propellant Based

#### Pressurized Metered Dose Inhalers (pMDIs)

- Breath synchronized
- Spacer designs
- Novel formulation technology



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## Inhalation Device Overview

### Vibrating mesh Omron, Pari eFlow, Nektar

- Portable nebulizers
- Shorter nebulization times
- “pMDI” substitute



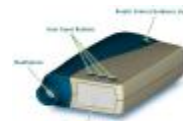
### Ultrasound Oriol, Microdose

- Patient independent DPIs



### Extrusion Aradigm, RespiMat

- “pMDI” substitute
- Unit dose / efficiency



### Electronic Atomization Kurve

- Nasal controlled particle dispersion

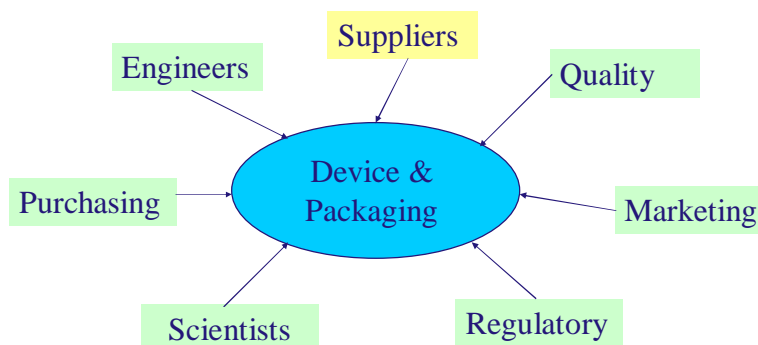


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## Inhalation Product Development

Design → Development → Commercialization



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## Inhalation Device Materials

### Pharmaceutical Inhalation Device Components

- Drug Container
- Dosing mechanism (for multi-dose products)
- Dispersing mechanism
- Mouthpiece

### Use of Plastics in Inhalation Devices

- Housing/Container
- Functional/mechanical components
- Aesthetic components

### Other Materials Commonly Used

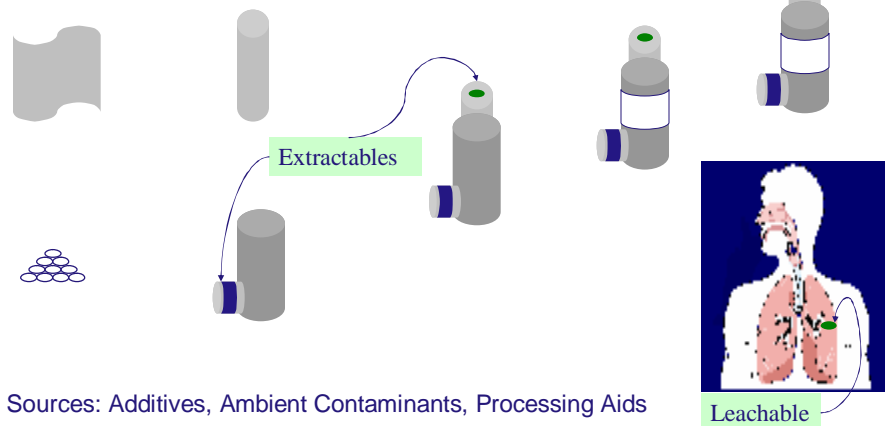
- Elastomers—valves and seals
- Metal—containers; functional/mechanical components

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## Life of An Extractable

Material Supplier → Component Mfr → Filler/Assembler → Pharm Mfr → Patient

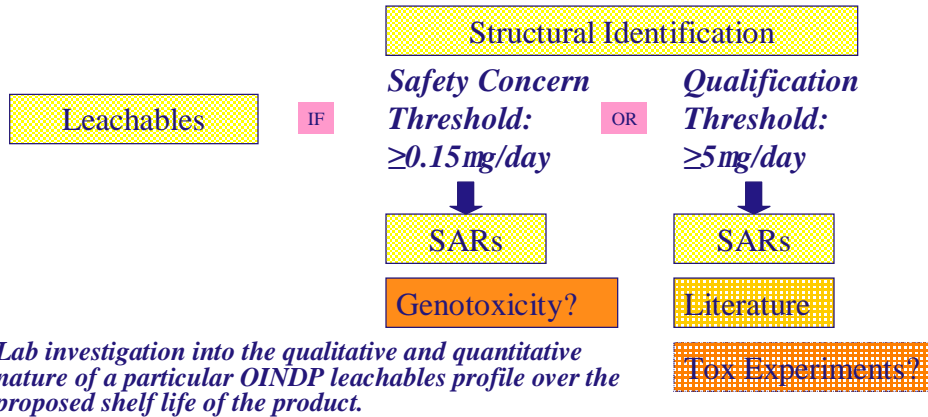


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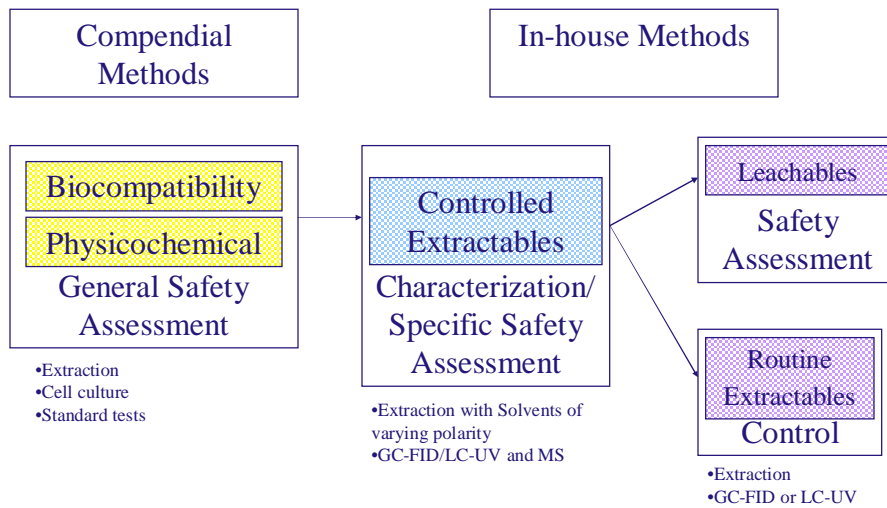
# Leachables—Safety Assessment

Product = Drug + Pkg + Device

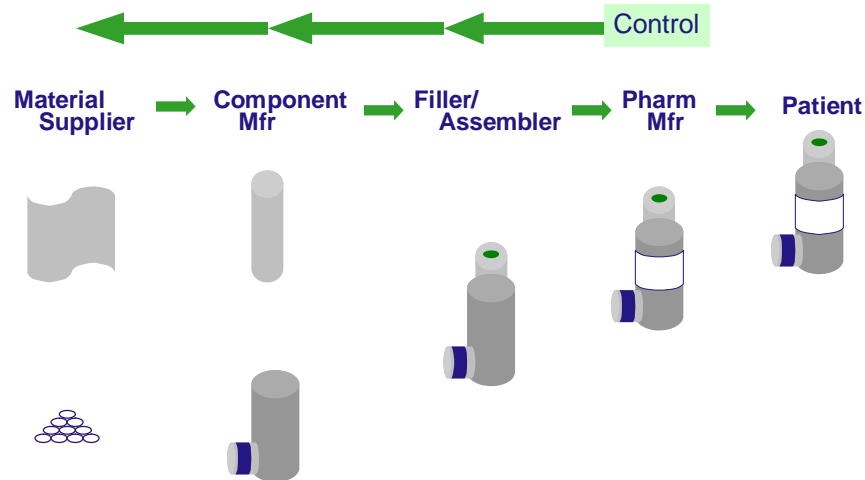


(Ref: Recommendations from PQRI Leachables & Extractables Workshop, Dec 2005)

# Drug or Mucosal Contacting Components—Extractables for Characterization/Control



## Control of Extractables



Sources: Additives, Ambient Contaminants, Processing Aids

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## Component Extractables Controls— MDI/DPI Draft Guidance 1998

### Section III.G.2.a

“Critical components of the DPI are defined as those that contact either the patient (i.e., the mouthpiece) or the formulation, components that affect the mechanics of the overall performance of the device, or any necessary protective packaging.”

### Section III.G.2.c

“...the applicant should establish discriminatory test methods and set appropriate acceptance criteria of the extractable profile(s) for routine testing of incoming individual critical device components”

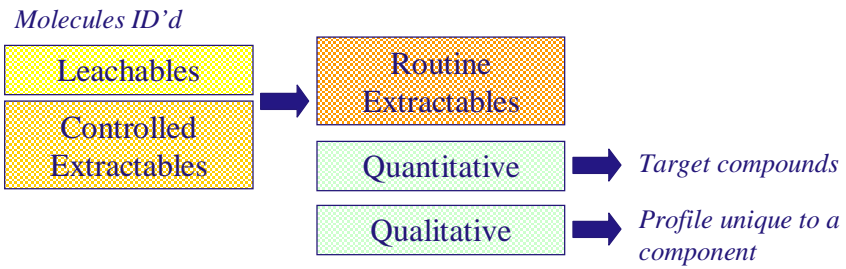
### Section III.G.2.e

“Specifications should include...qualitative and quantitative extraction profile(s) of each individual component for indirect control of composition...”

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## Routine Extractables Method Development



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## Routine Extractables Methodology

- ▣ Sample preparation
- ▣ Extraction
- ▣ Analysis

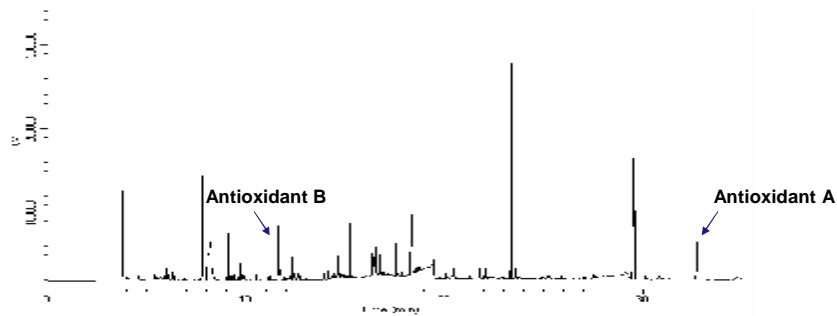


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## Routine Extractables Example

- u Sample preparation: ground polypropylene
- u Extraction: ASE
- u Analysis: GC-FID

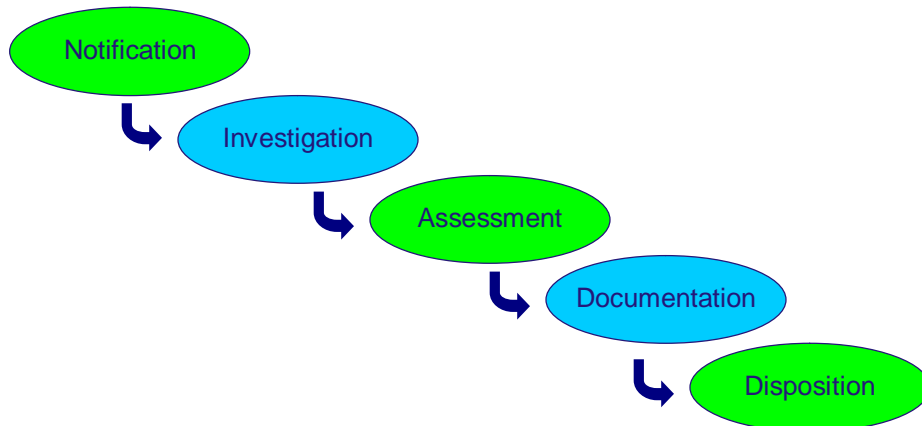


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## Component Extractables Controls— Managing the Unexpected

- u What happens when extractables are used to control quality?



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## Component Extractables Controls— Managing the Unexpected

### u What happens when extractables are used to control quality?

#### u Case Study #1

- Device component – elastomer
- Target compound level above upper limit
- Lab investigation shows result is accurate
- Batch rejected

#### u Case Study #2

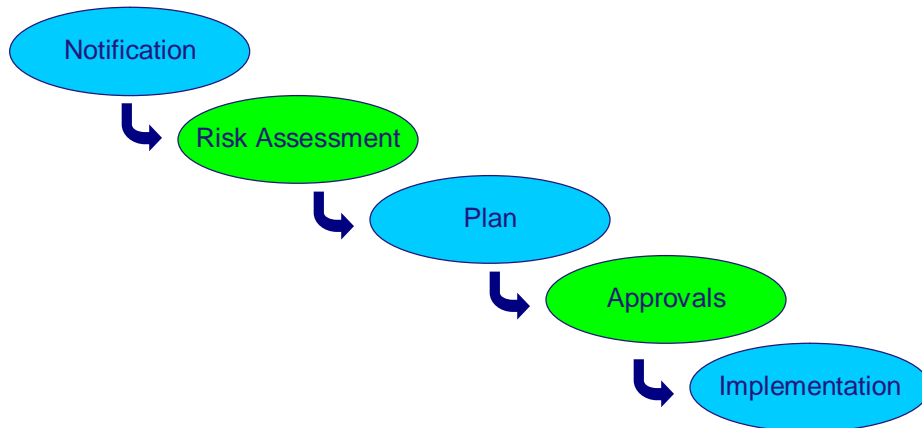
- Device component – elastomer
- Peak previously below threshold appears above threshold in chromatogram
- Lab investigation reveals identity of peak
- No concern based on safety evaluation of compound
- Batch released

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## Component Extractables Controls— Managing the Unexpected

### u What happens when a material change is anticipated?

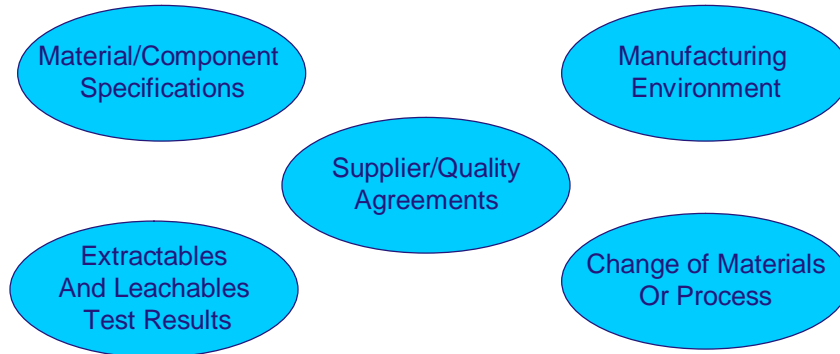


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## Component Extractables Controls— Managing the Challenges Together

### u Opportunities for interactions between OINDP Manufacturers and Suppliers

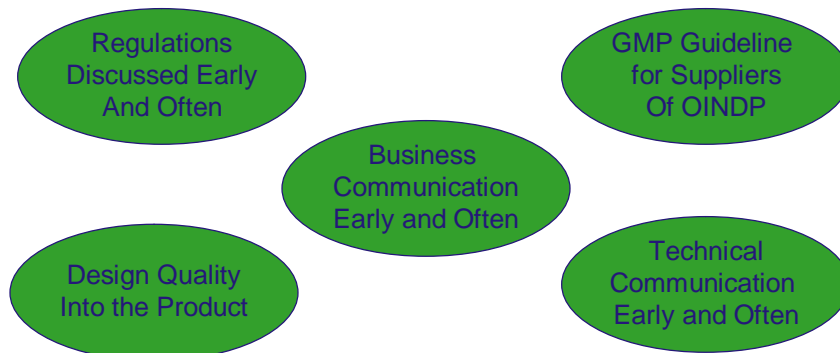


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## Component Extractables Controls— Managing the Challenges Together

### u Types of interactions between OINDP Manufacturers and Suppliers

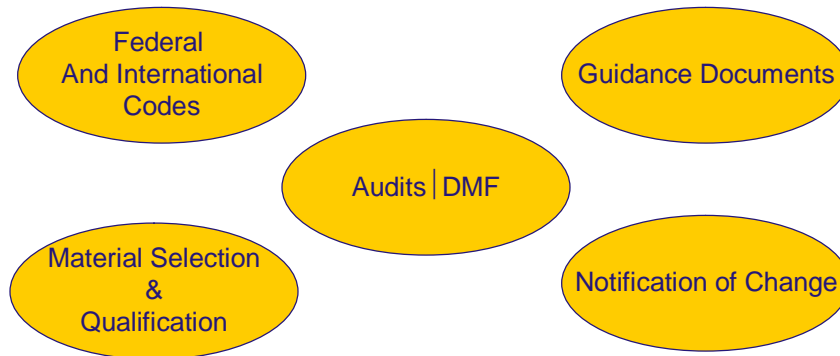


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## Component Extractables Controls— Managing the Challenges Together

### u Tools of the Industry



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## Summary

- u A steady pipeline of Inhalation Products means a continuous need for high quality materials
- u Extractables testing is expected as an indirect control of material consistency
- u Recent recommendations call for very low levels of any detectable compounds, which in turn demand high levels of control over material and process throughout the supply chain
- u Several opportunities exist for open communication between OINDP manufacturers and suppliers throughout the development and commercialization of OINDP
- u A variety of tools are now available to ensure quality of OINDPs from the beginning of a product concept through commercialization

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