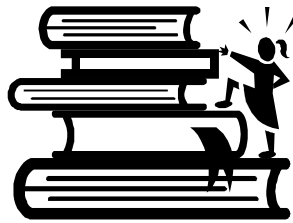




# Role of the IPAC-RS GMP Guideline in Promoting OINDP Component Quality

*Barbara Falco, Kos Pharmaceuticals*



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## Outline

### ÿ Background

ÿ Why is OINDP component quality important?

ÿ What is the IPAC-RS Guideline?

ÿ Using the IPAC-RS Guideline to promote  
OINDP component quality

ÿ Benefits of Using the IPAC-RS Guideline

ÿ Next Steps & Take Home Points

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2



## Background

*Why is OINDP component quality important?  
What is the IPAC-RS Guideline?*

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## Acronyms



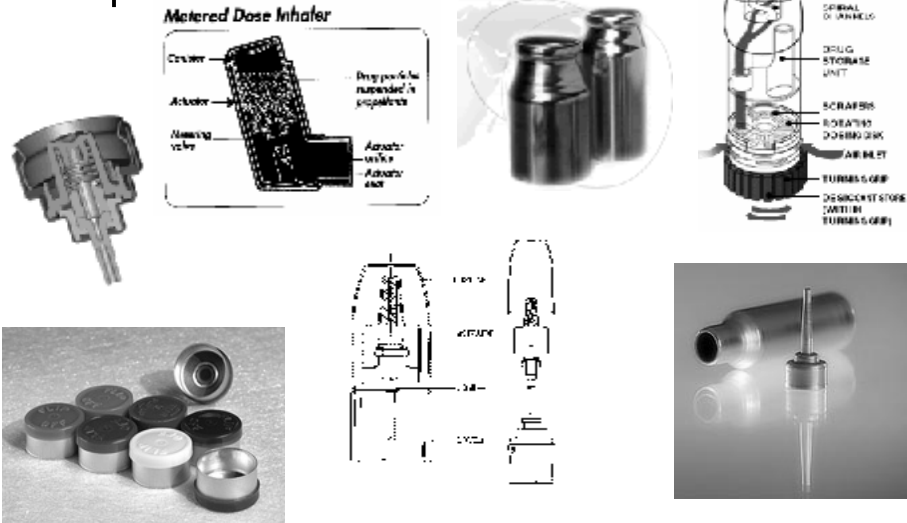
- OINDP manufacturer: Pharmaceutical company that manufactures and sells OINDP
- N-1 Supplier (aka OINDP component supplier): Supplier of components or materials directly to the OINDP manufacturer
- N-2 Supplier: Supplier of materials to n-1 supplier

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# OINDP Components

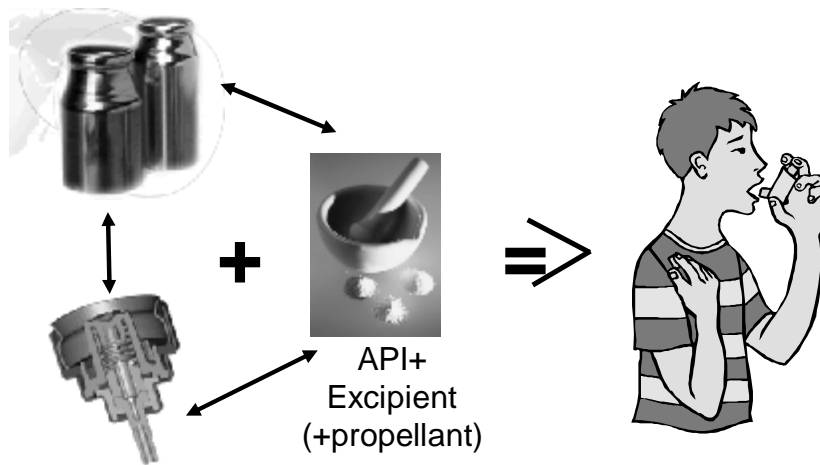


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Sources of Images:  
IPAC-RS SQC WG and suppliers' public catalogues  
5



# OINDP Functionality



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## FDA Regulation of OINDP

- FDA regulates the drug product (device/components + formulation) produced by pharma, not suppliers of drug product components
- HOWEVER:
  - FDA Guidances for OINDP set forth expectations for the quality of OINDP components
  - Many CMC tests are impacted by component quality



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## Example: MDI Component Quality from MDI/DPI Draft Guidance

“...potential leaching of compounds from the elastomeric and plastic components...is a serious concern that should be addressed.

Therefore, the composition and quality of the materials used in the manufacture of the container and closure system components should be carefully selected.”

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## CMC Tests for OINDP in FDA Guidances

### Component quality plays a critical role in many CMC tests

1. *Assessment of Packaging Materials*
2. *Appearance / Description of Product*
3. *Color*
4. *Identification (2 specific tests)*
5. *Chiral Specificity, if applicable*
6. *Microbial Limits*
7. *Microbial Challenge*
8. *Water Content*
9. *Alcohol Assay if applicable*
10. *Content Assay*
11. *Assay for other excipients*
12. *Net Content Weight*
13. *Leak Rate*
14. *Pressure Testing*
15. *Spray Pattern*
16. *Plume Geometry*
17. *Valve Delivery (Shot Weight)*
18. *Dose Content Uniformity (uniformity of API delivered from mouthpiece)*
19. *Dose Content Uniformity Through Canister Life (API delivered from mouthpiece at beginning, middle, and end of canister)*
20. *Particle Size Distribution of API – Mass Balance and Groupings (Cascade Impactor)*
21. *Effect of Storage on Particle Size Distribution*
22. *Microscopic Evaluation (particle size, morphology, crystallinity, amorphous forms, agglomerates, etc.)*
23. *Foreign particles (enumeration, characterization)*
24. *Leachables*
25. *Extractables*
26. *Dissolved metals*
27. *Impurities and Degradation Products*
28. *Number of Doses Delivered*
29. *Effect of Resting Time*
30. *Priming and Re-priming*
31. *Drug Deposition on Mouthpiece and/or Other Accessories*
32. *Profiling of Actuators Near Canister Exhaustion*
33. *In vitro Dose Proportionality (multi-strength doses)*
34. *Effect of Flow Rates*

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## Why the IPAC-RS GMP Guideline?

Typical OINDP includes many different components interacting with each other formulation

Components are critical to delivery of the drug product

No FDA regulation of suppliers

IPAC-RS GMP Guideline for Suppliers of OINDP Components

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10



## What is the IPAC-RS GMP Guideline?

- 3-in-1 Guideline:
  - ISO 9001:2000
  - PS 9000:2001
  - IPAC-RS GMP Guideline
- Provides tools to achieve and maintain compliance with GMPs
  - In alignment with 21 CFR 210-211 and 820



## What is the IPAC-RS GMP Guideline?

- Global Applicability
  - The Guideline takes into account regulations and expectations for OINDP in all regions
  - The Guideline is intended to be used by suppliers in all regions





## Development of IPAC-RS GMP Guideline

- IPAC-RS Supplier QC Working Group surveyed OINDP suppliers and manufacturers regarding QA/QC practices and expectations
- Based on survey results, Working Group determined a need for clear guidance on GMP for OINDP components, and identified critical areas of GMP
- Working Group drafted text addressing each area
  - Reviewed text to ensure harmonization with and no duplication of existing quality guidelines
- Based on supplier suggestion, Working Group decided to incorporate IPAC-RS Guideline into PS 9000 Guideline for Pharmaceutical Packaging Materials

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13



## Application of the IPAC-RS GMP Guideline

- Applies to n-1 suppliers of components for OINDP not regulated by FDA or other device regulations, e.g.,
  - Canister / reservoir / primary package
  - Actuator,
  - Pump, etc.
- Does not address devices or device manufacturers
- n-2 and n-3 suppliers who supply to n-1 suppliers are encouraged to read and follow Guideline

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14



## Key Sections of IPAC-RS GMP Guideline



- OINDP Components/Sub-components
- Quality Unit
- Change Control
- Supply & Quality Agreements
- Extractables
- Cleaning & Foreign Particulates

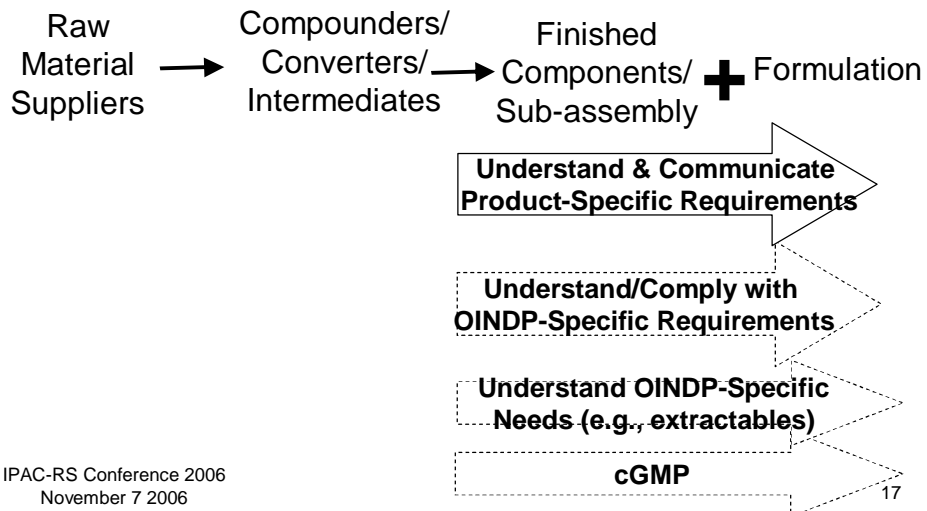


## Using the IPAC-RS Guideline to Promote OINDP Component Quality





## Current Paradigm for OINDP



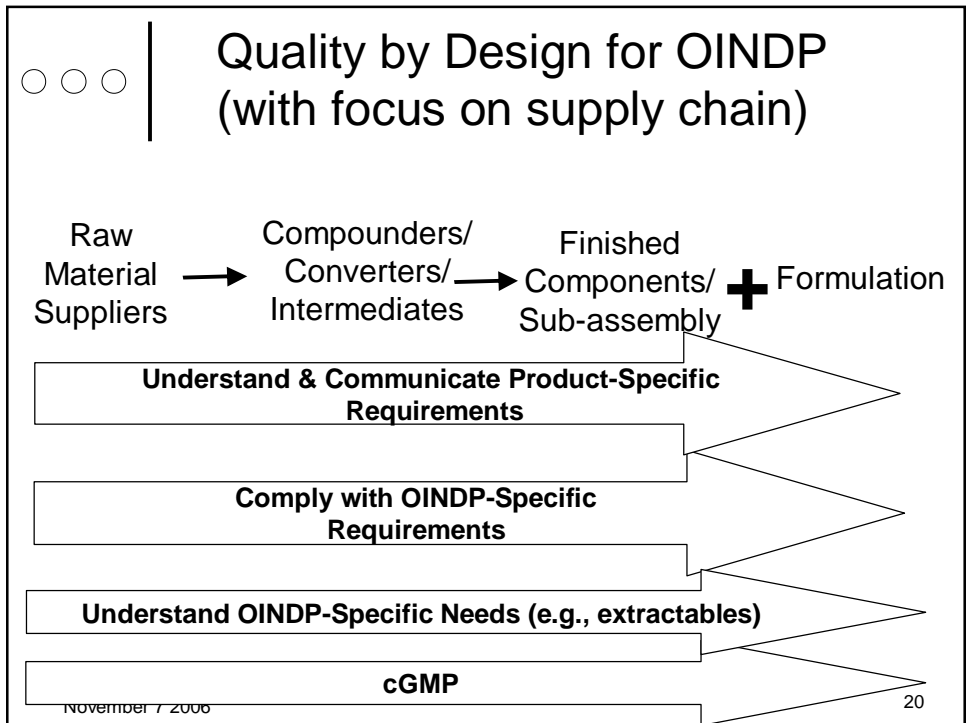
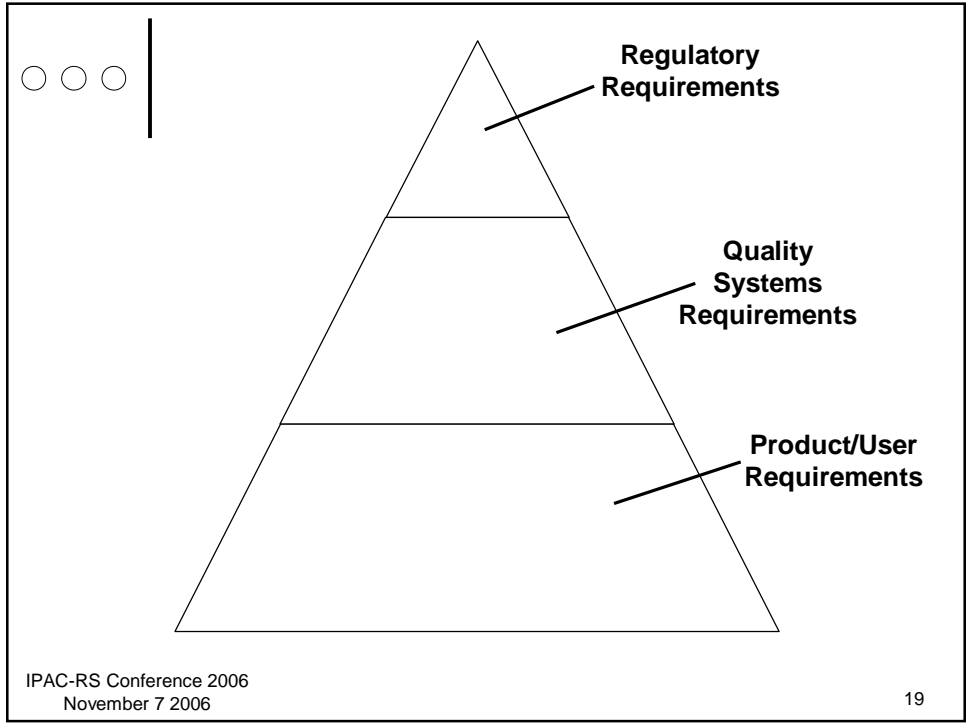
## Quality By Design

If we want to build quality in, we need to begin at the beginning...



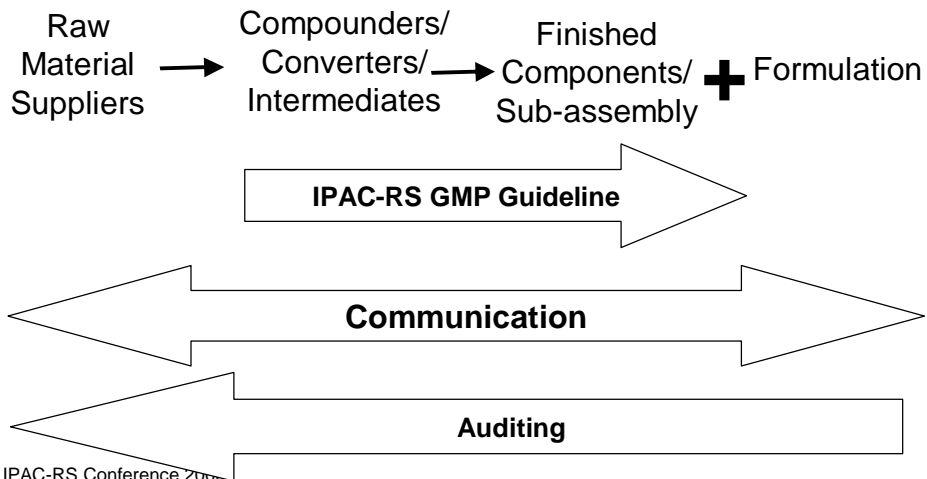
**Rubber tree**

*Image courtesy of Kew Royal Botanic Gardens*





## Quality by Design for OINDP (with focus on supply chain)



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21



## Using the IPAC-RS Guideline to Achieve Quality Product: OINDP Manufacturers

- Provide the Guideline to the appropriate individuals at your company and encourage them to review and use it
  - QA & QC
  - Purchasing
  - Component Selection
- Make your suppliers aware of the Guideline and encourage them to use it
- Use the Guideline in your discussions with current and potential suppliers
- N-1 suppliers may be audited by their customers against IPAC-RS, PS 9000, and ISO 9001 sections

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22



## Using the IPAC-RS Guideline to Achieve Quality Product: OINDP Manufacturers

- Communicate with your suppliers and ensure that they have the necessary information from you regarding how their component will be used and your requirements for their component
- Communicate with your suppliers to determine whether they need assistance in meeting the Guideline's requirements

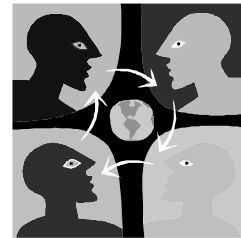


## Using the IPAC-RS Guideline to Achieve Quality Product: N-1 Suppliers

- Read and follow the contents of the IPAC-RS, PS 9000, and ISO 9001 sections of the Guideline
- Guideline and supplier:
  - Many requirements allows room for variation based on needs of customer are "as defined by the customer," "as agreed between the supplier and the customer" or "where applicable"
- Communicate with your customers
- Communicate with your suppliers (n-2 suppliers)



Notice a theme?



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## N-2/N-3 Suppliers

- N-2/N-3 suppliers are encouraged to read and follow the Guideline where applicable/appropriate.
- Topics of particular importance at the N-2/N-3 level include:
  - Change control
  - Cleaning and material changeover procedures
- N-2/N-3 suppliers should communicate with customers regarding which sections of the Guideline may apply
- N-2/N-3 suppliers should communicate with customers to understand the use of their materials and the impact of potential changes

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26



## Benefits of Using the Guideline

- **Regulators:**
  - More confidence in OINDP container closure system and device components
- **Pharma:**
  - Consistent, high quality components
  - Better relationship with suppliers
  - Fewer supply chain events
- **Suppliers:**
  - Clear understanding of customers' expectations
  - More consistent expectations and audits
  - Better relationship with customers
  - Improved quality systems



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## Benefits of Using the Guideline

- **Patients:**
  - Better products



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28



## Next Steps

- IPAC-RS working with ISO to incorporate IPAC-RS GMP Guideline into next version of ISO 15378 Standard for Pharmaceutical Packaging Materials
- Promoting use of the Guideline by OINDP manufacturers and suppliers to achieve:
  - Harmonized expectations of suppliers
  - Better understanding by suppliers of OINDP needs with respect to GMP
  - High & consistent quality components
  - High & consistent quality OINDP
  - Fewer supply chain problems

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29



## Promoting Awareness

- Second IPAC-RS Workshop on OINDP Supplier GMP
  - February 14, 2007 in Chicago, IL
  - Will address application and use of IPAC-RS GMP Guideline
  - In-depth presentations by suppliers and OINDP manufacturers on critical areas of GMP
- IPAC-RS Symposium on Extractables in Materials for OINDP
  - February 13, 2007 in Chicago, IL
  - Promote & improve understanding of particular materials requirements for OINDP, i.e., extractables
  - Promote dialogue between all parts of the OINDP component supply chain
- For more information and registration, visit [www.ipacrs.com/supplier.html](http://www.ipacrs.com/supplier.html)
- Workshop on IPAC-RS Guideline at RDD Europe 2007 ([www.rddonline.com](http://www.rddonline.com))

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30



## Take Home Point: Use It or Lose It!

The IPAC-RS Guideline will not be effective unless we (Industry) use it. Use of the Guideline increases its effectiveness and influence



## Take Home Point:

# WIN - WIN - WIN





## Conclusion

- OINDP components are critical to the quality and performance of OINDP
- IPAC-RS hopes that its GMP Guideline will be helpful in standardizing and clarifying quality expectations for OINDP component suppliers
- IPAC-RS expects that OINDP manufacturers will begin using the Guideline as an auditing standard for their suppliers
- The IPAC-RS Guideline does not replace supplier-customer communication and in fact emphasizes the importance of such communication

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33



## IPAC-RS Supplier QC Working Group and Guideline Contributors

<b>Boehringer Ingelheim</b>	Ray Oksala	<b>Pfizer</b>	Suzette McTigue
<b>Eli Lilly*</b>	Ben Dai Marcia Arentz	<b>Presspart*</b>	Bert Calvert Susan Hall Annette Thompson
<b>KOS</b>	Barbara Falco, <b>Chair</b>		
<b>Nektar</b>	Kenneth McCain*	<b>Schering- Plough</b>	Michael Lusty*
<b>Novartis</b>	Rainer Frueh	<b>Valois</b>	Valerie Leveque,* <b>Vice-chair</b> Amandine Tagliente
<b>Novo Nordisk</b>	Lisa Erdös		
<b>Sanofi- Aventis</b>	Linda Nield	<b>West</b>	Fran DeGrazio Tom Gaspar

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\*Former WG members

34