



Extractables – Role of Supplier/Pharmaceutical Company Relationship

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Overview

- ⌄ **Supplier/Pharmaceutical Company Relationship**
- ⌄ **Protection of Information**
- ⌄ **Supplier and Pharmaceutical Company Partnership**
- ⌄ **Establishing Limits for Extractables**
- ⌄ **Example – Good Relationship**
- ⌄ **Take Home Messages**

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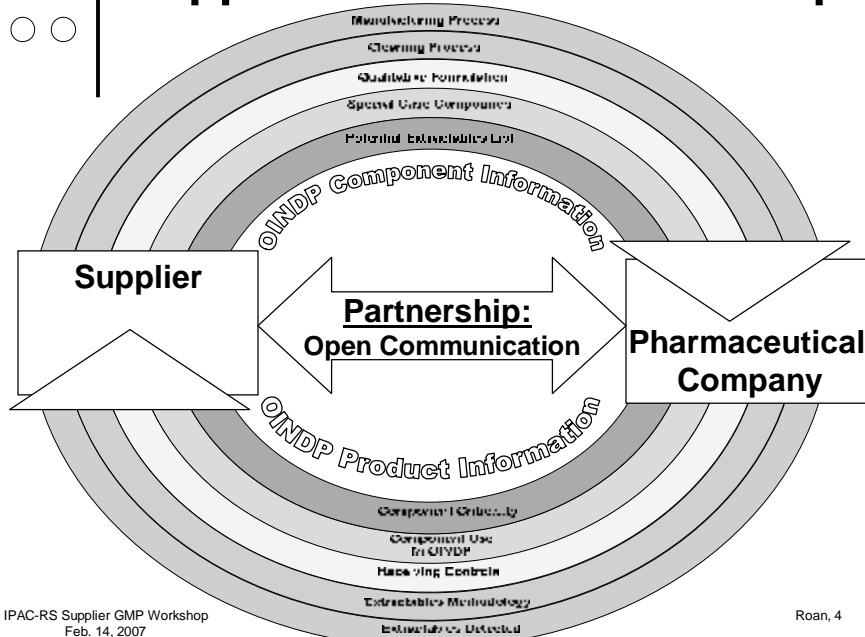


Supplier/Pharma Relationship

- ⌘ **Need to balance the proprietary nature of the formulation against the pharmaceutical company's desire for information**
 - | **Supplier is interested in protecting their proprietary formulation**
 - | **Pharmaceutical company is interested in understanding the materials in their product, which facilitates product and process understanding**



Supplier/Pharma Relationship





Recommended Information Shared by Supplier

☒ Manufacturing Process



- | How components are measured and added to the batch can impact extractables levels
- | Type of manufacturing process used can provide information on potential presence of special case compounds

☒ Cleaning Process

- | How the equipment is cleaned between batches may have an impact on extractables



Recommended Information Shared by Supplier (continued)

☒ Qualitative Formulation



- | Base Polymer, including any known additives
- | Additives (antioxidants, plasticizers, stabilizers)
- | Pigment Packages

☒ Special Case Compounds

- | Potential presence of these compounds require specialized testing to verify presence and levels, if seen
 - Nitrosamines
 - Polynuclear aromatic hydrocarbons
 - 2-Mercaptobenzothiazole



Recommended Information Shared by Supplier (continued)

⌄ Potential Extractables List



- | Based on previous testing of the component/formulation, or
- | Theoretically based on formulation, manufacturing and cleaning processes



Recommended Information Shared by Pharmaceutical Company

⌄ Extractables Detected

- | Results from controlled extraction experiments
- | Experimental conditions used

⌄ Extractables Methodology

- | Description of method details, if method already developed
- | Description of planned methodology, if method is in development

⌄ Receiving Controls

- | Description of tests which the pharmaceutical company will employ in order to accept the component as well as limits, if established



Recommended Information Shared by Pharmaceutical Company (continued)



- ⌘ **Component Use in OINDP**
 - | The role of the component in the OINDP
 - | Design/Functional requirements for the component
 - | Expectations of component performance and use life
 - | Contact with Formulation or Patient
- ⌘ **Component Criticality**
 - | Level of criticality drives testing, including whether extractables are required



Protection of Information



- ⌘ **Quality Agreements**
 - | Agreements between the supplier and the pharmaceutical company relating to quality and regulatory systems
- ⌘ **Non-Disclosure Agreements**
 - | Legally binding confidentiality agreements between the companies
 - | Can be established between multiple parties, i.e., 4-way Non-Disclosure Agreements
- ⌘ **DMFs**
 - | Confidential submission made by supplier to the FDA. Reference is made to DMFs in IND/NDA submissions
 - Recommend using DMFs for the actual trade secret information, and sharing the remainder of the non-trade secret processing and control information with the pharmaceutical company



Supplier and Pharmaceutical Company Partnership

- ⊕ Partnership is based on open communication and sharing of information
- ⊕ Communication should be initiated prior to selecting the material for use in the OINDP and throughout the product development lifecycle
- ⊕ Communication should include peers from the supplier and the pharmaceutical company, i.e.,
 - | Engineers/staff scientists working with their counterparts
 - | Regulatory/QA working with their counterparts

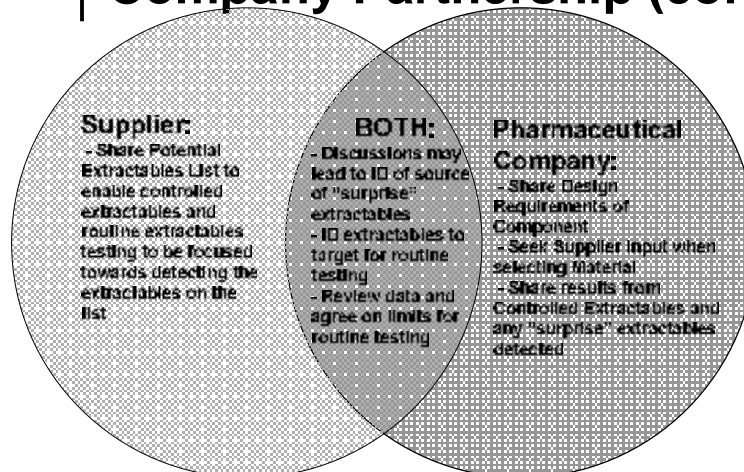


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Supplier and Pharmaceutical Company Partnership (cont'd)



Mutual benefits when the suppliers and pharmaceutical companies work together!

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Establishing Limits for Extractables – *Best Case*

- ⌄ **Source known for each extractable (quantitative and qualitative) to be specified**
- ⌄ **Control of the source of each extractable is within the control of the supplier (directly or through controls with n-2 suppliers)**
- ⌄ **Limits established based on historical data and design of experiments (enhanced product knowledge)**
- ⌄ **Increased assurance for supplier and pharmaceutical company that component will meet these limits, as the extractables are understood and controlled**



An Example of a Good Relationship – Problem Solving



- ⌄ **Extractable detected in product, but was not purposefully added by supplier**
- ⌄ **Face to face meetings between supplier and pharmaceutical company project teams**
- ⌄ **Reviewed all ingredients in formulation in detail**
- ⌄ **Source of extractable determined to be from a low level impurity in a solvent used in the manufacturing process**
- ⌄ **Result = greater product and process understanding by both companies**



Take Home Messages



- ☞ **Suppliers and pharmaceutical companies should be at the table throughout product development**

- ☞ **Suppliers and pharmaceutical companies have valuable information which should be shared with one another**

- ☞ **Working together increases the product knowledge, which leads to more meaningful extractables controls**



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Questions?