Extractables – Role of Supplier/Pharmaceutical Company Relationship

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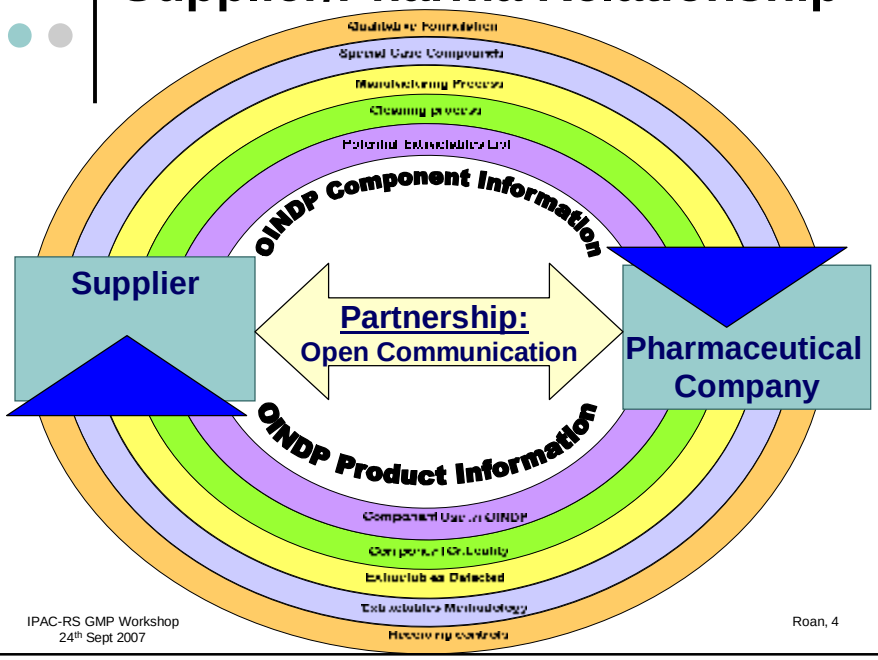
Overview

- Supplier/Pharmaceutical Company Relationship
- Protection of Information
- Forming Partnerships
- Example – Good Relationship
- Take Home Messages

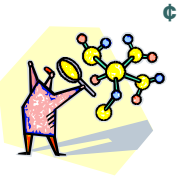
Supplier/Pharma Relationship

- 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

Supplier/Pharma Relationship



Recommended Information Shared by Supplier



- 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
    - Nitrosamines
    - Polynuclear aromatic hydrocarbons
    - 2-Mercaptobenzothiazole

Recommended Information Shared by Supplier

- Manufacturing Process
  - Measurement and addition of components to the batch can impact extractables levels
  - Manufacturing process can provide info 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

- 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

- 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

Recommended Information Shared by Pharmaceutical Company

- Extractables Detected
  - Results from controlled extraction experiments
  - Experimental conditions used
- Extractables Methodology
  - Description of method details
  - Description of planned methodology
- Receiving Controls
  - Description of tests the pharmaceutical company will employ to accept the component (as well as limits)

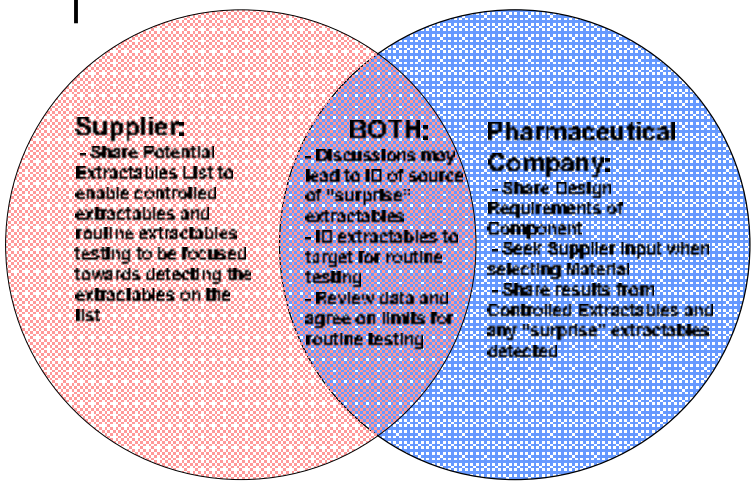
Protection of Information

- 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

Forming Partnerships

- 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 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

Forming Partnerships



Mutual benefits when the suppliers and pharmaceutical companies work together!

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 (in detail) all ingredients in formulation and manufacturing process
- Source of extractable determined as 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 <u>throughout product lifecycle</u>
- Suppliers and pharmaceutical companies have <u>valuable information which should be shared with one another</u>
- Working together <u>increases</u> the product knowledge, which leads to more <u>meaningful extractables controls</u>

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Questions?