OTC Program – Elemental Impurities Lifecycle; the Next Step

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E.I. Lifecycle Program

Outline:

- Current Status of the E.I. Program
- Key Challenges
  - Materials
  - Change Control
  - External Partners
- Lifecycle Program Strategy
- Other Considerations

E.I. Lifecycle Program

What is the current status of the E.I. Program?

- We are Past the Development Phase and moving into the Infancy.
- Each Company has a program - A documented Risk Assessment that demonstrates Compliance with E.I. for each product.
  - Internal Documents or Approved Supplier Documents associated with purchased products
  - A combination of the two for Repackaged Products.
- In 2018 each company will transition to a Lifecycle Program

E.I. Lifecycle Program

Key Challenges associated with E.I.

- Variation in the level of information from Suppliers
- Limited Regulatory Feedback
  - How much Data, Analytical L.O.Q, Control Strategy,..
  - to be derived through Filings – ANDA, NDA, PAF, CBE-30…
- Process / Material Changes
  - Internal
  - External
  - Formulations
  - Packaging Materials
  - Manufacturing Equipment

- Build in a process where changes can be incorporated quickly / effectively

E.I. Lifecycle Program

Raw Materials

Challenge: Without a defined standard it is difficult to obtain information. If the only elements being managed are the “known” impurities, are you managing the “unknown”?

Tools:

- Supply Agreements: Include an E.I. Assessment
- Change Notification Process: Include an E.I. Assessment
- Information Request: Comparison to existing material received – a change in the base line. Define which Elements as dictated by your Product needs.
- If you cannot obtain information from the Supplier, perform your own analysis.

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Formulation Changes (Major / Alternate Source Projects)

Challenge: Update all corresponding documents / process to include an E.I. assessment. Impact to the Product Risk Assessment.

Tools: Define Requirements Associated with each Change Type:

- Raw Material: define minimum data requirements for an Alternate Source Project.
- Alternate Equipment: define your approach to both the justification and the documentation.
- Product Risk Assessment: define when the RA needs to be revised
  - Minimum data requirements associated with new or revised Formulations.
  - Do you develop a Waiver Program associated with low risk changes.
    - Material Category (dye, flavor,…), Source Type (Natural versus synthetic), % changes of ingredients, n-1, literature search,…
  - Changes can be logistically burdensome. If you have a “one stop” document, do all changes drive a document revision?

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External Partners

Challenge: Defining Roles and Responsibilities. Clarify Expectations. Is this defined in your Supply Agreements?

Tools:

- Define your Company's Expectations:
  - Contract Manufacturers of Bulk Product
  - Repackaging Operations
  - Direct Buy Finished Goods
- Direct Buy:
  - Assumption: The Supplier will own the E.I. Product Risk Assessment.
    - What is the program? Review during audit, certificate of conformance, approve the Product Risk Assessment…

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External Partners (Cont.)

- Repackaging Operations:
  - Similar to Direct Buy, however as a repackaging operations does your Company issue a “Secondary Product Risk Assessment” to encompass the repackaging process when product is moved into a new direct contact component? Has this been defined?
- Contract Manufacturing of Bulk Product
  - Define responsibilities associated with the Product Risk Assessment. Contract Manufacturer and the Finished Product Distributor.
    - Formulation / Raw Material Assessment
    - Equipment Assessment
    - Packaging Assessment
    - Product Risk Assessment

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Lifecycle Program – how far do you go?

Challenge: How does a Company insure that there are not changes associated with the Supply Chain or Internal Processing. A onetime risk assessment or an ongoing monitoring program?

Tools:

- Material Program:
  - Link to a CofA Testing program.
  - Define materials that might be included in the program based upon the risk. Natural source RM, does the Supplier have a program, % of formulation,…
  - Have a process by which the data is assessed against past raw material assessments and the Product Risk Assessments.
  - Keep segmented from the Product Risk Assessment document – avoids unnecessary revisions.

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Lifecycle Program (cont)

Tools:

- Product Program:
  - Could be a challenge if there is not internal analytical capability.
  - Link into other change control programs.
    - Qualification Batches
    - Alternate Packaging Configurations
    - Pre-Market Stability Program
- The Goal is to Confirm the status of the existing Product Risk Assessments

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Other Considerations

- Regulatory Feedback:
  - Rely on your Product Risk Assessments to support the program.
  - Understand the potential that feedback will triggers changes. Implement as an improvement to the current program.
- Local Regulations:
  - Be aware of local regulations and build the linkage to the Product Risk Assessment.
  - Keep as a companion document / process.
- Flavors, Colorants, & Dyes: Take into account the risk based upon % of formulation.
- Supply Agreements: Include an E.I. Assessment
- Change Notification Process: Include an E.I. Assessment

E.I. Lifecycle Program

Thank You