Extractable/Leachable assessment of manufacturing equipment components-OPQ’ s perspective

AAM GRx+Biosims 2024 Conference

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October 22, 2024

Disclaimer

This presentation reflects the views of the author and should not be interpreted to represent FDA's view or policies.

Regulation

- **Regulation for safety assessment of manufacturing equipment components: 21CFR211.65(a)**
- *Equipment shall be constructed so that surfaces that contact components, in-process materials, or drug products* ***shall not be reactive****,* ***additive****, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.*

FDA Guidance

- Many FDA's guidance contain recommendations on Extractables and Leachables (E/L) associated with container/closure system (CCS). The principles and approaches are generally applicable to manufacturing equipment.
- Container Closure Systems for Packaging Human Drugs and Biologics
- Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products — Chemistry, Manufacturing, and Controls Documentation
- Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products--Quality Considerations (draft)
- Quality Considerations for Topical Ophthalmic Drug Products (draft)
- Transdermal and Topical Delivery Systems - Product Development and Quality Considerations (draft)

ICH guidance

- ICH Q3E: ICH Q3E: Guideline for Extractables and Leachables (E&L) (in developing, see concept paper at ICH website)

USP chapters

- <665> PLASTIC COMPONENTS AND SYSTEMS USED TO MANUFACTURE PHARMACEUTICAL DRUG PRODUCTS AND BIOPHARMACEUTICAL DRUG SUBSTANCES AND PRODUCTS (official on 5/1/2026)
- <1665> CHARACTERIZATION AND QUALIFICATION OF PLASTIC COMPONENTS AND SYSTEMS USED TO MANUFACTURE PHARMACEUTICAL DRUG PRODUCTS AND BIOPHARMACEUTICAL DRUG SUBSTANCES AND PRODUCTS (currently official)
- <381> ELASTOMERIC COMPONENTS IN INJECTABLE PHARMACEUTICAL PRODUCT PACKAGING/DELIVERY SYSTEMS (currently official)

USP chapters (Cont.)

- <661> PLASTIC PACKAGING SYSTEMS AND THEIR MATERIALS OF CONSTRUCTION (currently official)
- <1663> ASSESSMENT OF EXTRACTABLES ASSOCIATED WITH PHARMACEUTICAL PACKAGING/DELIVERY SYSTEMS (currently official)
- <1664> ELASTOMERIC ASSESSMENT OF DRUG PRODUCT LEACHABLES ASSOCIATED WITH PHARMACEUTICAL PACKAGING/DELIVERY SYSTEMS (currently official)

Differences between E/L for equipment and that for CCS

- Shorter contacting time
- Smaller surface/volume
- No leachables from secondary sources
- Might be used under pressure (filters), elevated temperature or wider pH range (for intermediates)
- Multiple points of introduction
- Potential purging of leachables introduced at upstream (biologics)

Risk Based Approach

- Prior knowledge
  - prior use on approved product with similar formulation and manufacturing conditions
  - qualified vender provided extractable study
  - Life cycle management
- Dosage form
  - Solid vs liquid
- Route of administration
  - Orally administered drug product, compliance statement to the pertinent sections of 21 CFR for indirect food additive (composition, additives, fabrication, specifications, testing results, in-use limitations et al)


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