PDA Training Container Closure Systems

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- EU Directive
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3.1. Materials used for the manufacture of containers

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USP

<87> Biological reactivity tests - in-vitro
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<381> Elastomeric closures for injections
<660> Containers - Glass
<661> Plastic Packaging Systems and Their Materials of Construction
   <661.1> Plastic Materials of Construction
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Timeline for implementation of 661.1 and 661.2 is three years as of 01.05.2017. But for current submissions the updated sections can already be referenced (http://www.uspnf.com/notices/general-chapters-plastic)
USP

1207 Package Integrity Evaluation - Sterile Products
   1207.1 Package Integrity Testing in the Product Life Cycle - Test Method Selection and Validation
   1207.2 Package Integrity Leak Test Technologies
   1207.3 Package Seal Quality Test Technologies

1660 Evaluation of the inner surface durability of glass container

1661 Evaluation of plastic packaging systems and their materials of construction with respect to their user safety impact

1663 Assessment of extractables associated with pharmaceutical packaging/delivery systems

1664 Assessment of drug product leachables associated with pharmaceutical packaging/delivery systems
   1664.1 Orally inhaled and nasal drug products
USP - under revision

<661.4> Plastic Medical Devices Used to Deliver or Administer Pharmaceutical Products

<662> Containers – Metal

<665> Polymeric Components and Systems Used in the Manufacturing of Drug Products
JP - General Notices

- Numbering of container closure system relevant items changed
  - JP17: nos. 41 to 45
    - General definition of container closure system
    - Definition of well-closed container, tight container, and hermetic container
    - Definition of "light-resistant"
JP - General Rules for Preparations

  • Section (1): introduction
  • Section (2): principle of packaging of preparations
  • Section (3): packaging suitability
JP - General Tests, Processes and Apparatus

7. Test for Containers and Packaging Materials
   7.01 Test for Glass Containers for Injections
   7.02 Test Methods for Plastic Containers
   7.03 Test for Rubber Closure for Aqueous Infusions
JP - General informations

G7 Containers and Package

• Basic Requirements and Terms for the Packaging of Pharmaceutical Products
  • 1. Basic requirements of packaging for pharmaceutical products
    • 1.1. Suitability evaluation and requirements of packaging in the design stage
    • 1.2. Examples of suitability evaluation in the design stage of packaging for pharmaceutical products
  • 2. Terms of packaging for pharmaceutical products
    • 2.1. Basic terms
    • 2.2. Terms of individual packaging or containers
    • 2.3. Terms of packaging performance
  • 3. Reference
JP - General informations

G7 Containers and Package

• Basic Requirements for Plastic Containers for Pharmaceutical Use and Rubber Closures for Containers for Aqueous Infusions*
  • 1. Basic Requirements in Designing Containers for Pharmaceutical Use
    • 1.1. Plastic containers for pharmaceutical use
    • 1.2. Rubber closures for containers for aqueous infusions
  • 2. Toxicity Evaluation of Container at Design Stage
  • 3. Test Results to be recorded per Production Unit for Plastic containers for pharmaceutical use and Rubber closures for containers for aqueous infusions
    • 3.1. Plastic containers for pharmaceutical use
    • 3.2. Rubber closures for containers for aqueous infusions
Guidance for Industry

Container Closure Systems for Packaging Human Drugs and Biologics

CHEMISTRY, MANUFACTURING, AND CONTROLS DOCUMENTATION
Container Closure Systems for Packaging Human Drugs and Biologics

- This document is intended to provide guidance on general principles for submitting information on packaging materials used for human drugs and biologics.
- This guidance supersedes the FDA Guideline for Submitting Documentation for Packaging for Human Drugs and Biologics, issued in February 1987 and the packaging policy statement issued in a letter to industry dated June 30, 1995 from the Office of Generic Drugs.
- This guidance is not intended to describe the information that should be provided about packaging operations associated with drug product manufacture.
Container Closure Systems for Packaging Human Drugs and Biologics

• In general, this guidance does not suggest
  • ...specific test methods and acceptance criteria (except for references to The United States Pharmacopoeia methods),
  • ...a comprehensive list of tests.
• Details
  • ...should be determined based on good scientific principles for each specific container closure system for particular drug product formulations, dosage forms, and routes of administration.
• Acceptance criteria
  • ...should be based on actual data for particular packaging components and container closure systems, and they should be set to ensure batch-to-batch uniformity of packaging components.
Container Closure Systems for Packaging Human Drugs and Biologics

<table>
<thead>
<tr>
<th>Degree of Concern Associated with the Route of Administration</th>
<th>Likelihood of Packaging Component-Dosage Form Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>High: Ophthalmic Solutions and Suspensions; Transdermal Ointments and Patches; Nasal Aerosols and Sprays. Low: Oral Powders.</td>
</tr>
<tr>
<td>Low</td>
<td>Topical Solutions and Suspensions; Topical and Lingual Aerosols; Oral Solutions and Suspensions. Low: Oral Tablets and Oral (Hard and Soft Gelatin) Capsules.</td>
</tr>
</tbody>
</table>
Container Closure Systems for Packaging Human Drugs and Biologics

Packaging documentation

Description  Suitability  Quality  Stability

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Container Closure Systems for Packaging Human Drugs and Biologics

**Description**

Overall general description of the container closure system,

- For Each Packaging Component:
  - Name, product code, manufacturer, physical description
  - Materials of construction
  - Description of any additional treatments or preparations

**Protection**

- (By each component and/or the container closure system, as appropriate)
  - Light exposure
  - Moisture permeation & reactive gases (e.g., oxygen)
  - Solvent loss or leakage
  - Microbial contamination
  - Filth & Other

Suitability
Container Closure Systems for Packaging Human Drugs and Biologics

Suitability

Safety

• (for each material of construction, as appropriate)
  • Chemical composition of all plastics, elastomers, adhesives, etc.
  • Extractables, as appropriate for the material
  • Extraction/toxicological evaluation studies, as appropriate
  • Appropriate USP testing
  • Appropriate reference to the indirect food additive regulations (21 CFR 174-186)
  • Other studies as appropriate
Container Closure Systems for Packaging Human Drugs and Biologics

Suitability

• Compatibility
  • (for each component and/or the packaging system, as appropriate)
    • Component/dosage form interaction, USP methods are typically accepted
    • May also be addressed in post-approval stability studies

• Performance
  • (for the assembled packaging system)
    • Functionality and/or drug delivery, as appropriate
Container Closure Systems for Packaging Human Drugs and Biologics

**Quality Control**

For Each Packaging Component received by the Applicant:

- Applicant's tests and acceptance criteria
- Dimensional (drawing) and performance criteria
- Method to monitor consistency in composition, as appropriate

For Each Packaging Component provided by the Supplier:

- Description of the manufacturing process

**Stability**

See section III.C.4 for stability studies
Basic document for packaging development:

„Guideline on Plastic Immediate Packaging Materials“
(CPMP / QWP / 4359 / 03)
Guideline on Plastic Immediate Packaging Materials

Plastic packaging material for the active substance

- Solid active substance
- Non-solid active substance

Material described in Ph. Eur. or in the pharmacopoeia of a Member State and/or in accordance with Foodstuff

- yes
- no

- General information (3.1)
- Specification (3.2)
- Migration studies (5.1)
- General information (3.1)
- Specification (3.2)
- Extraction studies (4)
- Migration studies (5.1)
- Toxicological documentation (6)
Guideline on Plastic Immediate Packaging Materials

**Plastic packaging material for drug products**

- For oral and topical other than ophthalmic administration:
  - Solid dosage form
  - Non-solid dosage forms
    - Material described in Ph.Eur. or in the pharmacopoeia of a Member State and/or in accordance with Foodstuff legislation
      - yes
      - no
      - • General information (3.1)
        • Specification (3.2)
        • Interaction studies

- For inhalation, parenteral and ophthalmic administration:
  - Solid dosage form
  - Non-solid dosage forms
    - Material described in Ph.Eur. or in the pharmacopoeia of a Member State
      - yes
      - no
      - • General information (3.1)
        • Specification (3.2)
        • Interaction studies if necessary (5)
        • Toxicological information (6)
Guideline on Plastic Immediate Packaging Materials (CPMP/QWP/4359/03)

3 Data to be submitted

3.1 General information:

For all plastic materials that are used as immediate packaging material for active substances or medicinal products:

- the chemical name of the material;
- the chemical name(s) of any monomer used;

have to be indicated.

…..

For plastic materials intended for packaging of non-solid active substances:

- the complete qualitative composition of the plastic material (including additives, such as antioxidants, stabilisers, plasticisers, lubricants, solvents and/or dyes) if the active substance packaging material is not described in the European Pharmacopoeia or in the pharmacopoeia of a Member State, and the supplier cannot certify compliance with foodstuff legislation.
Guideline on Plastic Immediate Packaging Materials (CPMP/QWP/4359/03)

3 DATA TO BE SUBMITTED

3.1 General information:

For plastic materials used in packaging of non-solid medicinal products:

- the name of material supplier, if the medicinal product is intended for inhalation, parenteral or ophthalmic administration

- the complete qualitative composition of the plastic material as listed above, if the medicinal product is intended for inhalation, parenteral or ophthalmic administration, and the material is neither described in the European Pharmacopoeia, nor in the pharmacopoeia of a Member State or, additionally, in cases where the monograph authorises the use of several additives from which the manufacturer may choose one or several in defined limits. The qualitative composition should also be provided for non-compendial packaging materials used for non-solid medicinal product intended for oral or topical (except ophthalmic) administration, when the supplier cannot certify compliance with foodstuff legislation.
Guideline on Plastic Immediate Packaging Materials (CPMP/QWP/4359/03)

4 EXTRACTION STUDIES

5 INTERACTION STUDIES
   5.1 Migration Studies
   5.2 Sorption Studies

6 TOXICOLOGICAL INFORMATION/DOCUMENTATION

- General description of evaluation
- No methods
- No limits
- Considerations how to assess multi layer components/containers
Packaging related sections

Pharmaceutical Development, 3.2.P.2.4 and 3.2.P.2.6

• Description
• Suitability: protection, safety, compatibility (drug-container), performance
• Quality
• (Stability)

• Compatibility (e.g. with co-packed Medical Devices)
Packaging related sections

Pharmaceutical Development, 3.2.P.2.4
• P.2.4.01 Pharmaceutical Development – Container Closure System
• P.2.4.02 Container Closure Integrity
• P.2.4.03 Material Conformity
• P.2.4.04 Container Closure Functionality
• P.2.4.05 Compatibility of Drug Product with Packaging Materials
• P.2.4.06 Extraction Studies
• P.2.4.07 Migration Studies
• P.2.4.08 Sterilization of Packaging Materials
• P.2.6.01 Pharmaceutical Development – Compatibility (e.g. with co-packed Medical Devices)
Packaging related sections

Pharmaceutical Development, 3.2.P.2.4
Glass ampoule:
• P.2.4.01 Pharmaceutical Development – Container Closure System
• P.2.4.02 Container Closure Integrity
• P.2.4.03 Material Conformity
Packaging related sections

Pharmaceutical Development, 3.2.P.2.4
Glass vial with lyophilizate:
• P.2.4.01 Pharmaceutical Development – Container Closure System
• P.2.4.02 Container Closure Integrity
• P.2.4.03 Material Conformity
• P.2.4.05 Compatibility of Drug Product with Packaging Materials
• P.2.4.06 Extraction Studies
• P.2.4.07 Migration Studies
• P.2.4.08 Sterilization of Packaging Materials
Packaging related sections

Pharmaceutical Development, 3.2.P.2.4
Pre-filled syringe:
• P.2.4.01 Pharmaceutical Development – Container Closure System
• P.2.4.02 Container Closure Integrity
• P.2.4.03 Material Conformity
• P.2.4.04 Container Closure Functionality
• P.2.4.05 Compatibility of Drug Product with Packaging Materials
• P.2.4.06 Extraction Studies
• P.2.4.07 Migration Studies
• P.2.4.08 Sterilization of Packaging Materials
Packaging related sections

Drug Product Container, 3.2.P.7

- Description of container system and its components
- Drawings of container components
- Specifications and testing methods
- Batch data
Packaging related sections

Drug Product Container, 3.2.P.7

- P.7.01 Packaging Materials: describes the entire container system
- P.7.02 Description of Primary Packaging
- P.7.03 Packaging – Specification and Test Procedure
- P.7.04 Drawing of Packaging Materials
- P.7.05 Packaging – Batch Analyses
- P.7.20 Description of Secondary Packaging (non functional)
Packaging related sections

Drug Product Container, 3.2.P.7
Prefilled syringe:
- P.7.01 Packaging Materials: for the completed syringe
Per each component (barrel, plunger, tip-cap)
  - P.7.02 Description of Primary Packaging
  - P.7.03 Packaging – Specification and Test Procedure
  - P.7.04 Drawing of Packaging Materials
  - P.7.05 Packaging – Batch Analyses
- P.7.20 Description of Secondary Packaging: for the completed syringe
Thank you very much for your attention!!