# PDA Training Container Closure Systems

*Regulatory Background*

# Content

- Ph.Eur.
- USP
- JP
- FDA Guideline
- EU Directive
- Relevant eCTD sections

legally binding!

3.1. Materials used for the manufacture of containers

- 3.1.1. Materials for containers for human blood and blood components
  - 3.1.1.1. Materials based on plasticised Poly(vinyl chloride) for containers for human blood and blood components
  - 3.1.1.2. Materials based on plasticised Poly(vinyl chloride) for tubing used for the transfusion of blood and blood components
- 3.1.3. Polyolefines
- 3.1.4. Polyethylene without additives for containers for parenteral preparations and for ophthalmic preparations
- 3.1.5. Polyethylene with additives for containers for parenteral preparations and for ophthalmic preparations
- 3.1.6. Polypropylene for containers and closures for parenteral preparations and opthalmic preparations

legally binding!

3.1. Materials used for the manufacture of containers

- 3.1.7. Poly(ethylene-vinyl acetate) for containers and tubing for total parenteral nutrition preparations
- 3.1.8. Silicone oil used as a lubricant
- 3.1.9. Silicone elastomer for closures and tubing
- 3.1.10. Materials based on non-plasticised poly(vinyl chloride) for containers for non-injectable, aqueous solutions
- 3.1.11. Materials based on non-plasticised poly(vinyl chloride) for containers for dry dosage forms for oral administration
- 3.1.13. Plastic additives
- 3.1.14. Materials based on plasticised poly(vinyl chloride) for containers for aqueous solutions for intravenous infusion
- 3.1.15. Polyethylene terephthalate for containers for parenteral use

legally binding!

3.2. Containers

- 3.2.1. Glass containers for pharmaceutical use
- 3.2.2. Plastic containers and closures for pharmaceutical use
  - 3.2.2.1. Plastic containers for aqueous solutions for infusion
- 3.2.3. Sterile plastic containers for human blood and blood components
- 3.2.4. Empty sterile containers of plasticised poly(vinyl chloride) for human blood and blood components
- 3.2.5. Sterile containers of plasticised poly(vinyl chloride) for human blood containing anticoagulant solution
- 3.2.6. Sets for the transfusion of blood and blood components
- 3.2.8. Sterile single-use plastic syringes
- 3.2.9. Rubber closures for aqueous parenteral preparations, for powders and for freeze-dried powders

USP sections with up to three digits are mandatory for US sumissions

USP

<87> Biological reactivity tests - in-vitro

<88> Biological reactivity tests - in-vivo

<381> Elastomeric closures for injections

<660> Containers - Glass

<661> Plastic Packaging Systems and Their Materials of Construction

- <661.1> Plastic Materials of Construction
- <661.2> Plastic Packaging Systems for Pharmaceutical Use

<671> Containers – Performance Testing

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 sections with four digits are documenting state of the arts

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> Assessement 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

- JP17 – [2] General Notices for Packaging of Preparations
  - Section (1): introduction
  - Section (2): principle of packaging of preparations
  - Section (3): packaging suitability

legally binding!

## 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

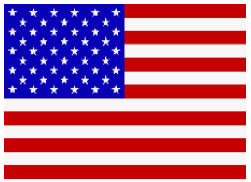
G7 Containers and Package

- 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



Key Guideline
for Development &
Quality Control

# 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.

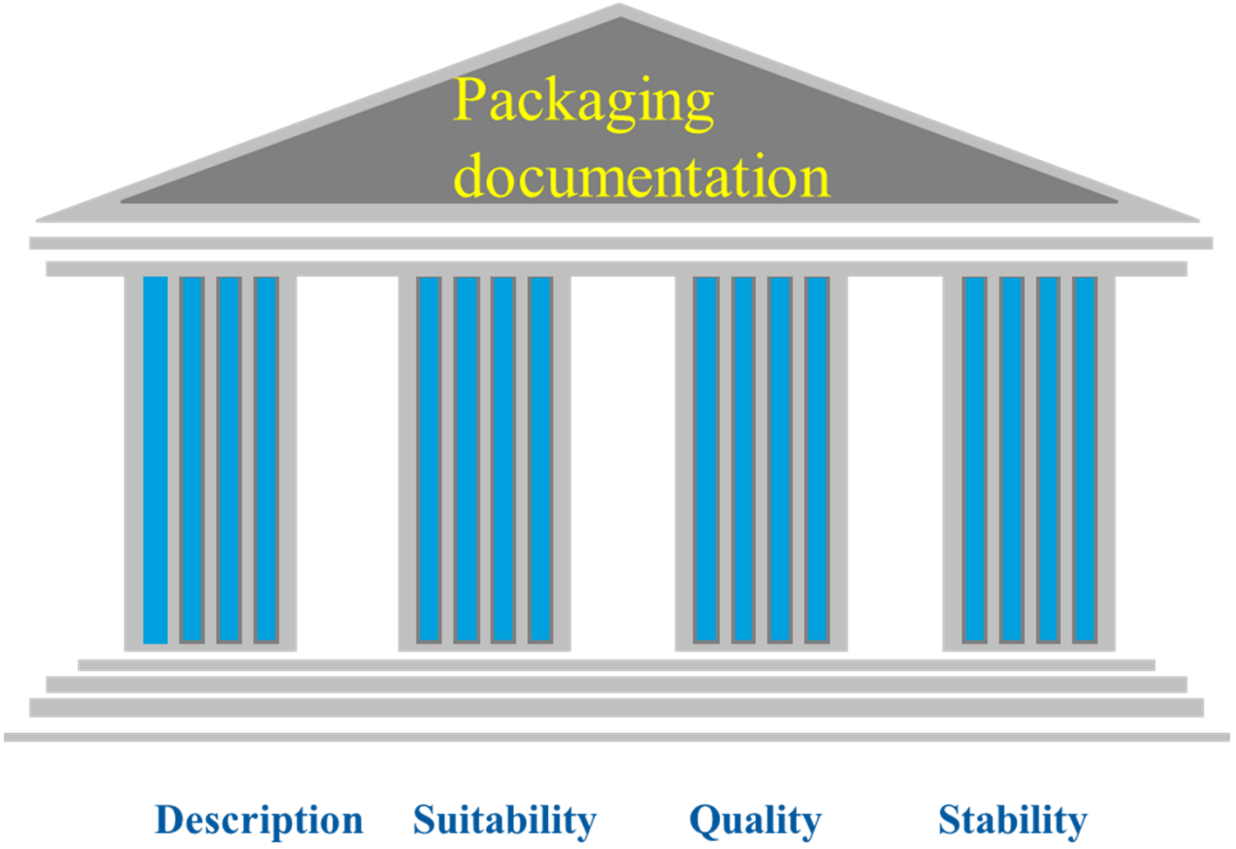
Container Closure Systems for Packaging Human Drugs and Biologics

- 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

| Degree of Concern Associated with the Route of Administration | Likelihood of Packaging Component-Dosage Form Interaction | | |
|---|---|---|---|
| | High | Medium | Low |
| Highest | Inhalation Aerosols and Solutions; Injections and Injectable Suspension | Sterile Powders and Powders for Injection; Inhalation Powders | |
| High | Ophthalmic Solutions and Suspensions; Transdermal Ointments and Patches; Nasal Aerosols and Sprays | | |
| low | Topical Solutions and Suspensions; Topical and Lingual Aerosols; Oral Solutions and Suspensions | Topical Powders; Oral Powders | Oral Tablets and Oral (Hard and Soft Gelatin) Capsules |

# Container Closure Systems for Packaging Human Drugs and Biologics



# 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

**Suitability**

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

# Container Closure Systems for Packaging Human Drugs and Biologics

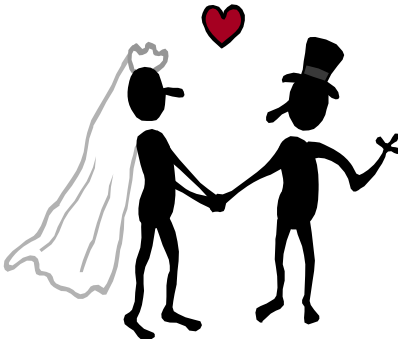
**Suitability**

Safety

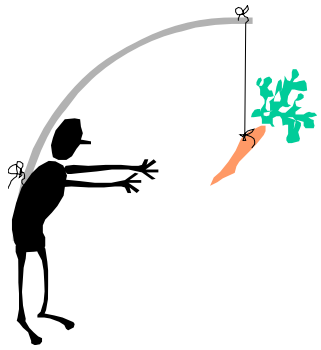
- (for each material of construction, as appropriate)
  - Chemical composition of all plastics, elastomers, adhesives, etc.
  - Extractables, as appropriate for the material
  - Extraction/toxicological evaluation studies, as appropriate
  - Appropriate USP testing
  - Appropriate reference to the indirect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

# Container Closure Systems for Packaging Human Drugs and Biologics

**Suitability**



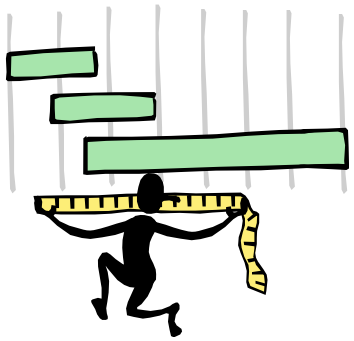
- Compatibility
- (for each component and/or the packaging system, as appropriate)
  - Component/dosage form interaction, USP methods are typically accepted
  - May also be addressed in post-approval stability studies



- 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

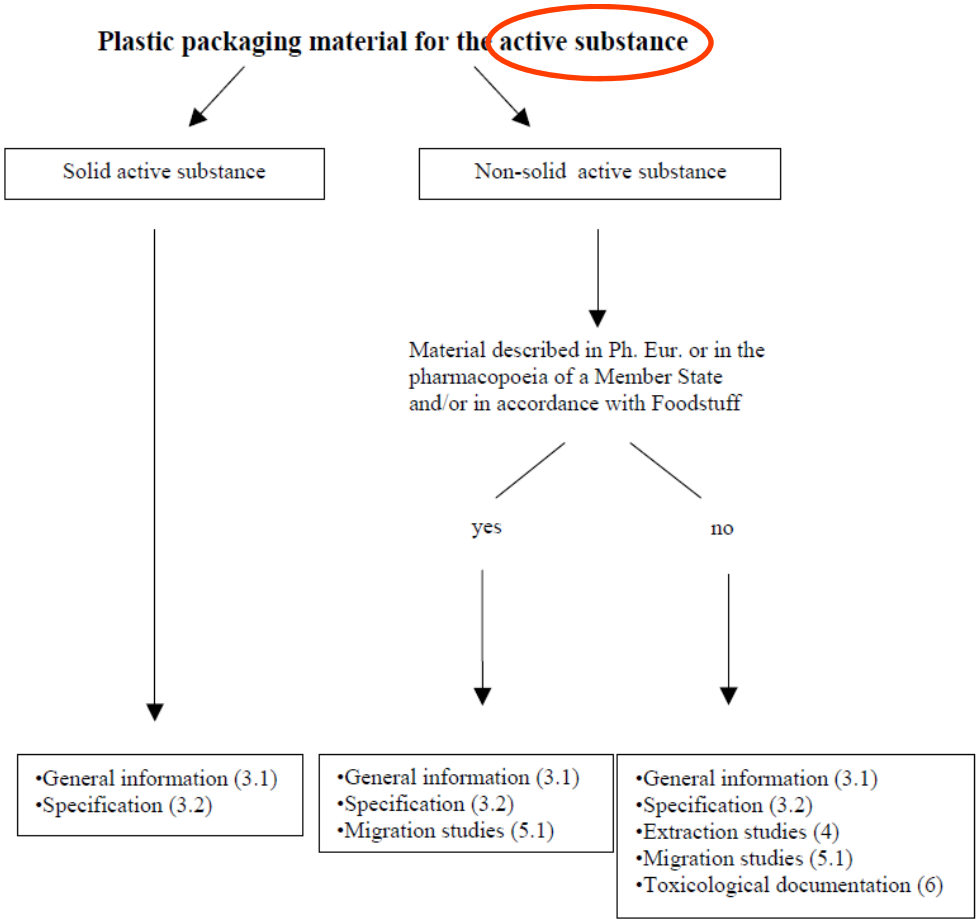
**Stability**

See section III.C.4 for stability studies

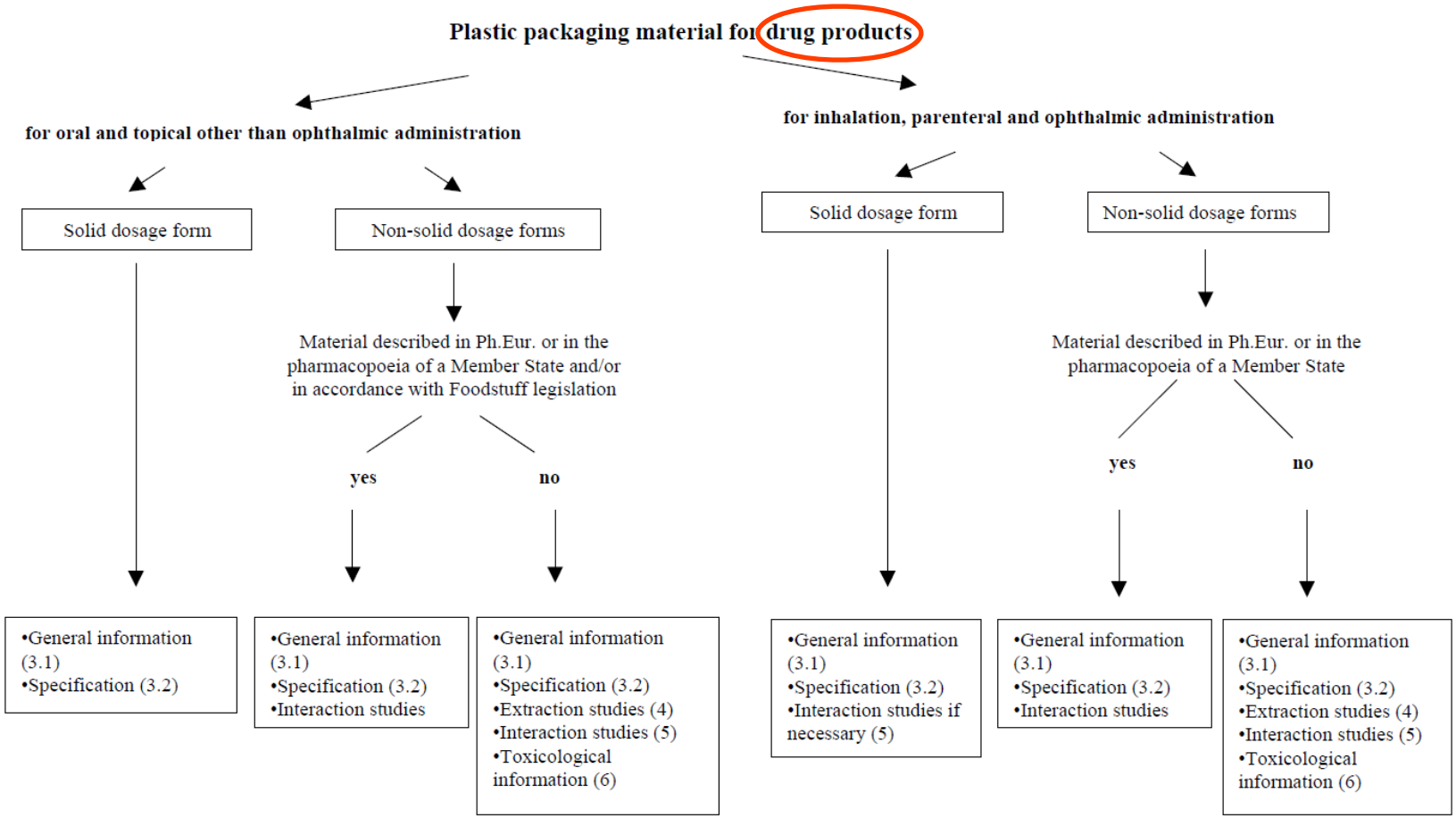
Basic document for packaging development:

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

# Guideline on Plastic Immediate Packaging Materials



# Guideline on Plastic Immediate Packaging Materials



## 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 decribed 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)

Practical example

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)

Practical example

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

Practical example

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

Practical example

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 und its components
- Drawings of container components
- Specifications and testing methods
- Batch data

Practical example

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

} per container component

- P.7.20 Description of Secondary Packaging (non functional)

Practical example

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!!