30 min

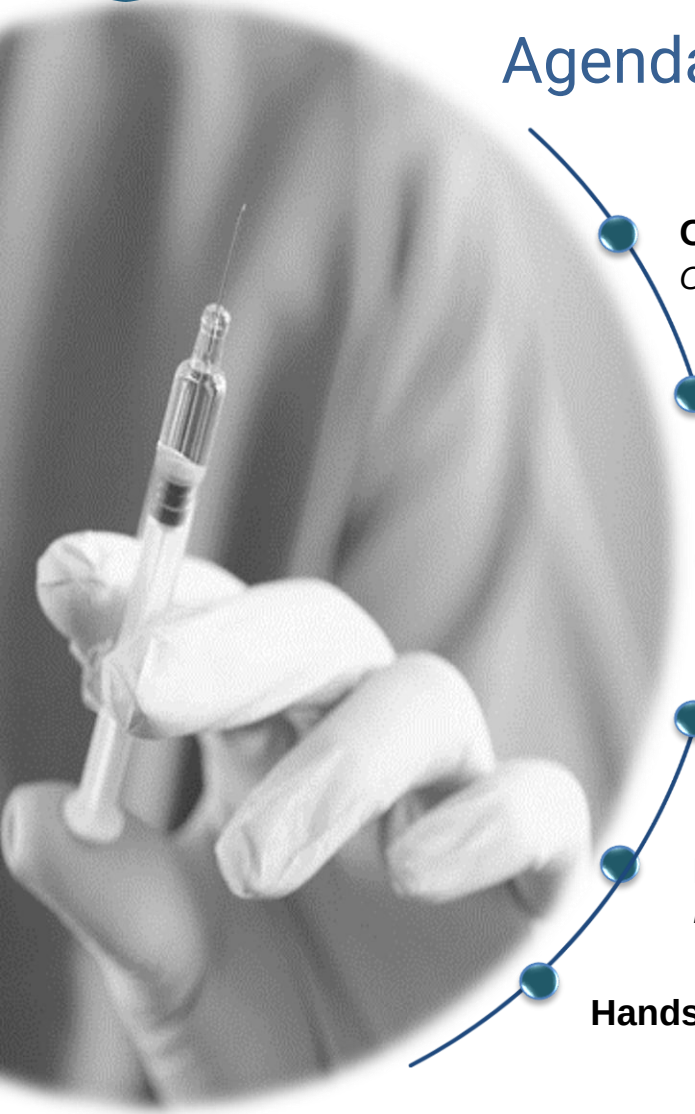
All about Pre-filled Syringe Systems

From Initial Development to Final Fill Finish

Christa Jansen-Otten
Bernd Zeiss

Basel, May 31st and June 1st 2022

Agenda – DAY 1



Overview and Introduction into Pre-filled Syringe Market
Overview & Trends • Stakeholders • User's perspective

Technical Aspects
Syringe • Plunger • Needle • Needle shield or Tip cap • Autoinjector • Regulatory guidelines and technical standards

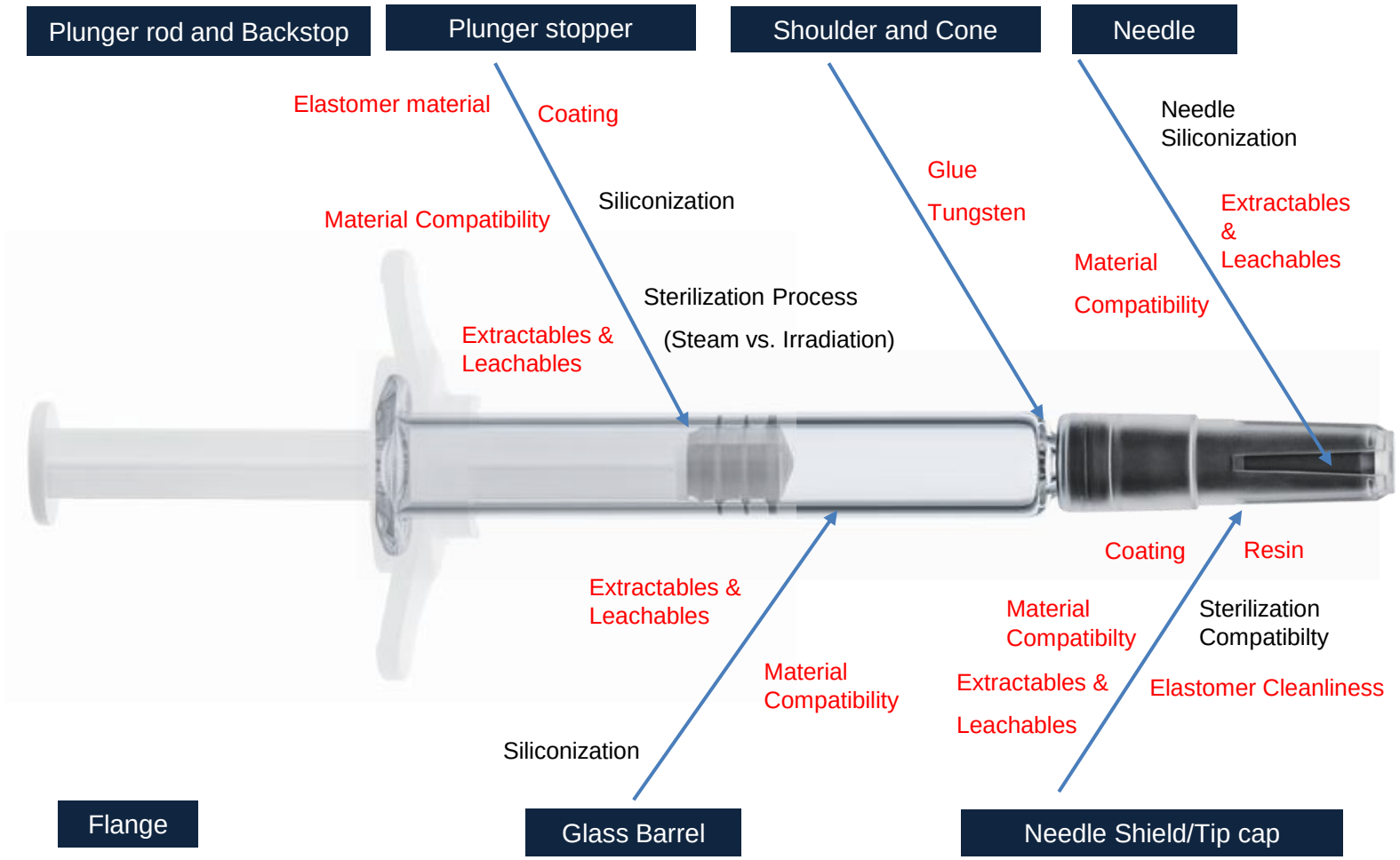
Overview & Introduction into Drug-Syringe Interactions
Aggregation • Degeneration • Oxidation • Viscosity • Bubbles

Overview & Introduction to manufacturing Process of PFS
Syringes Barrel Forming • Washing • Siliconization • Sterilization • Regulatory guidelines and technical standards …

Fill and Finish
Filling • Stoppering • Assembly • Technical Standards

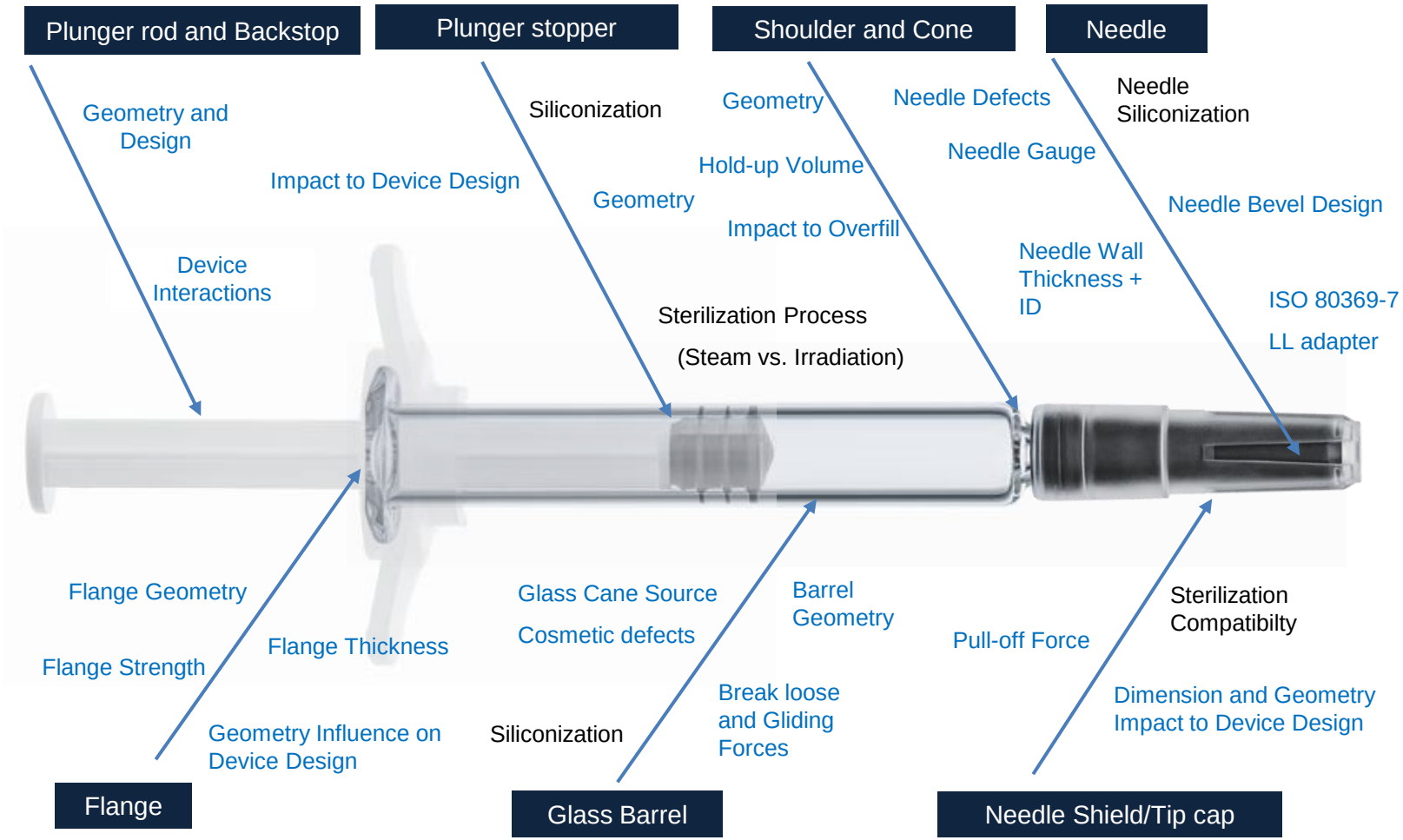
Hands-on Session 1

Pharmaco-chemical parameters



Adapted from David A. Post, Sherwin Shang, Shweta A. Raina,and William Szechinski. Development of Biopharmaceutical Drug-Device Products. PFS characterization and Interaction with Biologic Formulations. AAPS Advances in the Pharmaceutical Sciences Series 35, 2019 - 831 ff

Physical parameters



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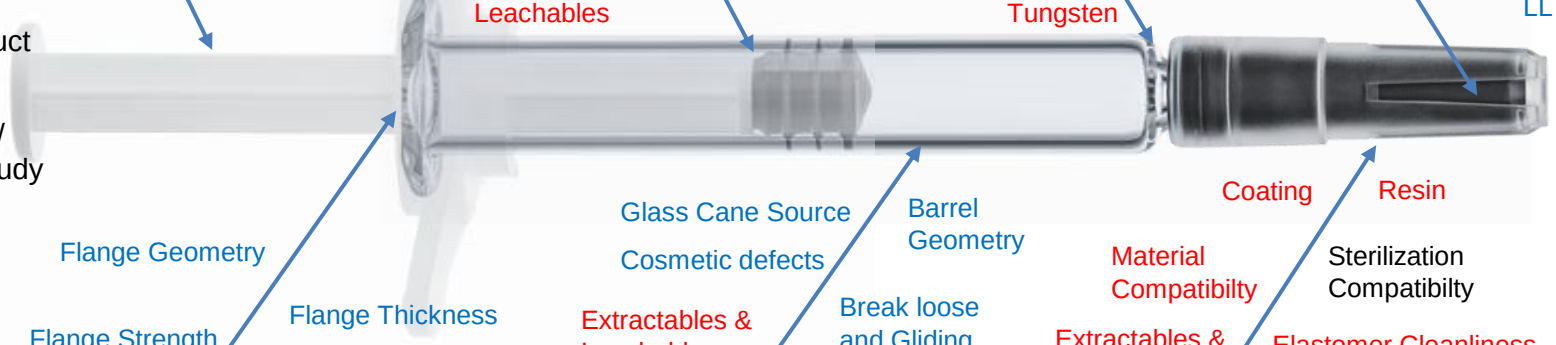
Pharmaco-chemical and physical parameters



Plunger rod and Backstop

Plunger stopper

Shoulder and Cone

Needle

Final Drug Product

Container Closure Integrity

Accuracy of Delivery Dose

Drug Product Stability

Shipping/ Vibration Study

Geometry and Design

Device Interactions

Elastomer material

Coating

Siliconization

Impact to Device Design

Material Compatibility

Geometry

Hold-up Volume

Impact to Overfill

Sterilization Process

(Steam vs. Irradiation)

Extractables & Leachables

Needle Defects

Needle Siliconization

Needle Gauge

Needle Bevel Design

Needle Wall Thickness + ID

Extractables & Leachables

Material Compatibility

Glue

Tungsten

ISO 80369-7

LL adapter

Flange Geometry

Flange Strength

Flange Thickness

Geometry Influence on Device Design

Flange

Glass Cane Source

Cosmetic defects

Extractables & Leachables

Siliconization

Material Compatibility

Barrel Geometry

Break loose and Gliding Forces

Glass Barrel

Coating

Resin

Material Compatibilty

Extractables & Leachables

Pull-off Force

Sterilization Compatibilty

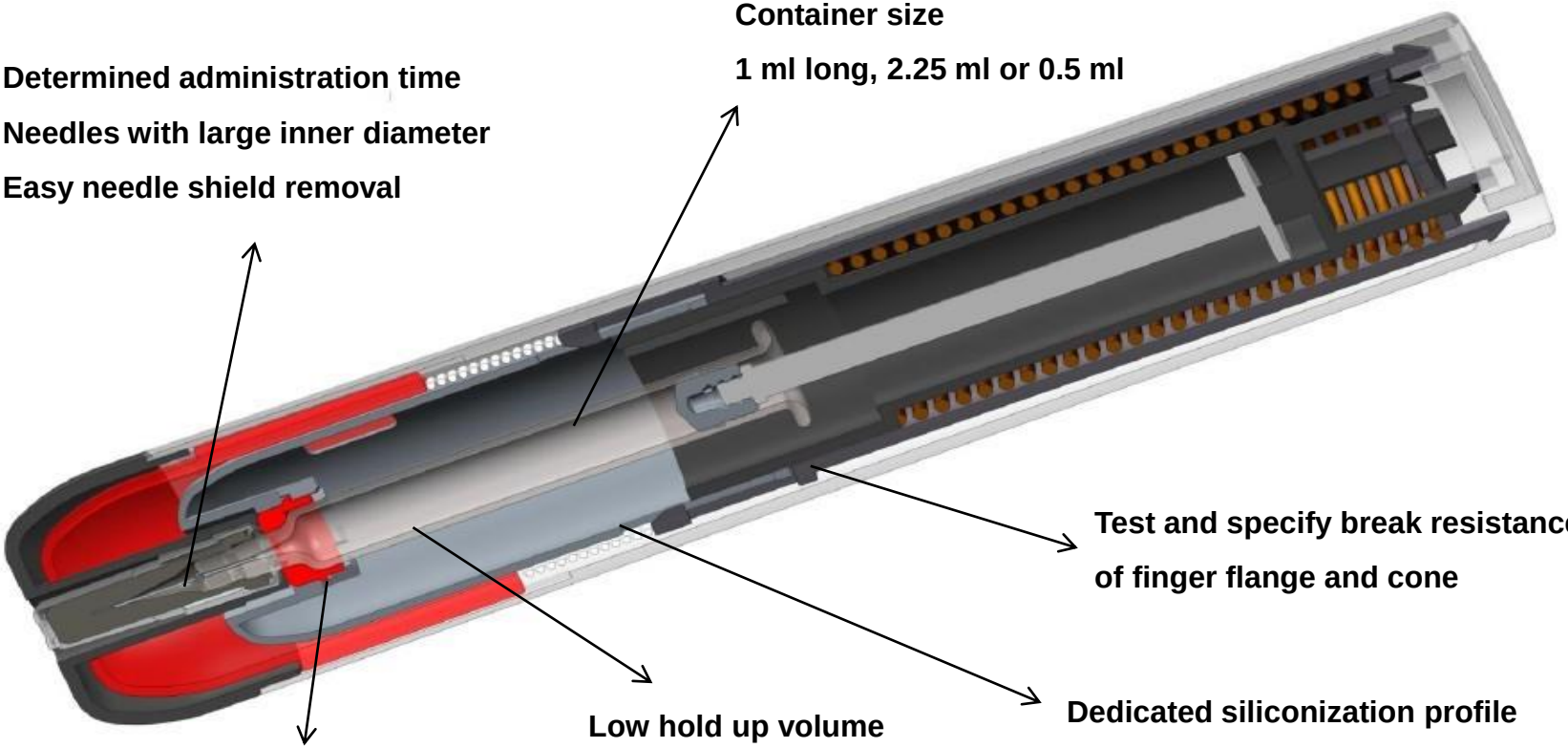
Elastomer Cleanliness

Dimension and Geometry Impact to Device Design

Needle Shield/Tip cap

Adapted from David A. Post, Sherwin Shang, Shweta A. Raina,and William Szechinski. Development of Biopharmaceutical Drug-Device Products. PFS characterization and Interaction with Biologic Formulations. AAPS Advances in the Pharmaceutical Sciences Series 35, 2019 - 831 ff

Syringe system with Autoinjector



Regulatory Guidelines

Mainly Dimensions and Test methods

Relevant norms and regulations

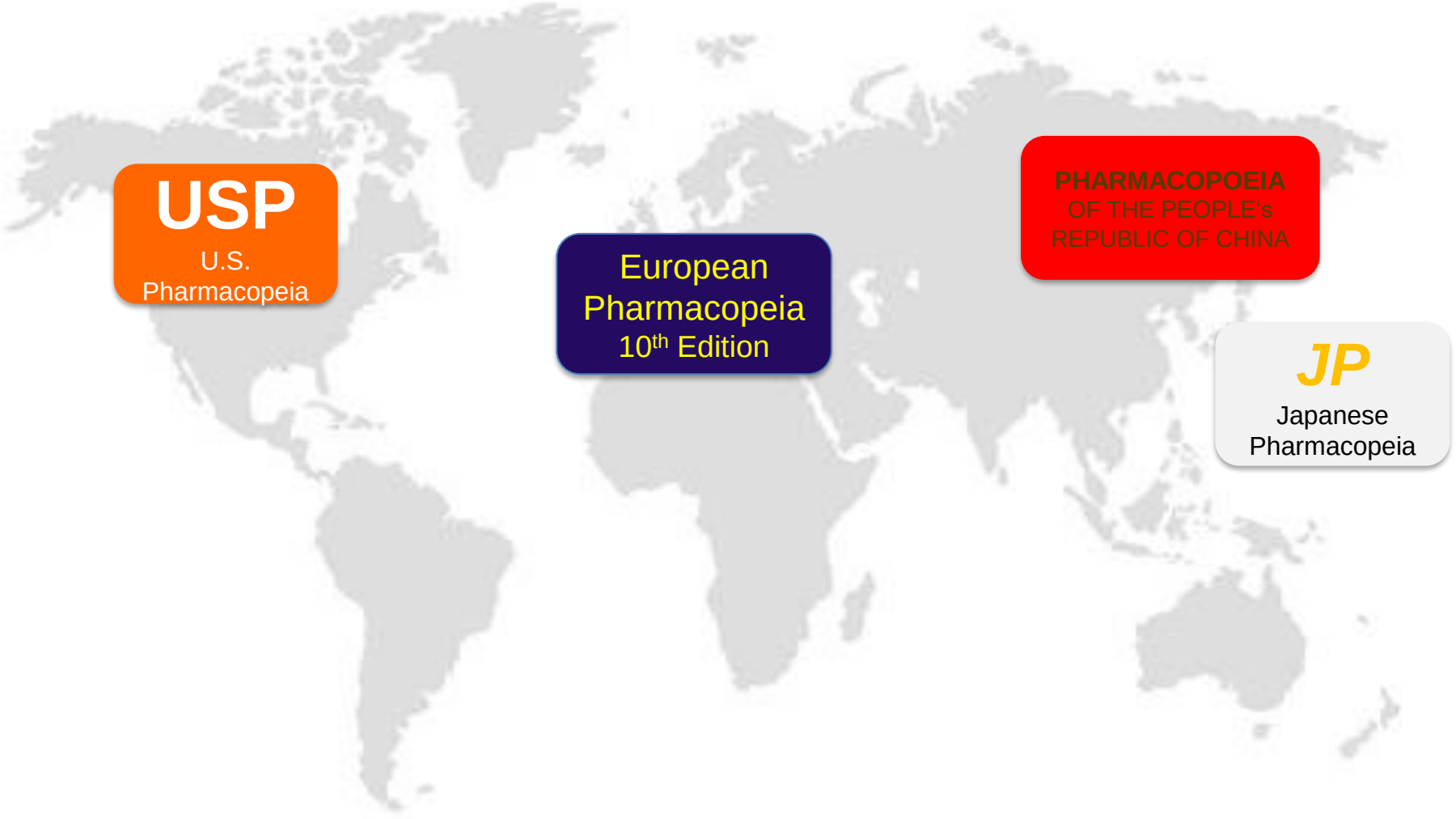
- **ISO 11040-4: Glass syringes ready for filling**
- **ISO 80369-7: Luer connectors**
- **ISO 11040-5: Plunger stoppers**
- ISO 11040-6: Plastic syringes ready for filling
- ISO 11040-7: Nest & tub
- **ISO 11040-8: Test methods for finished prefilled syringes**

- ISO 13926-1: Pen cartridges
- ISO 9187-1: Ampoules
- ISO 8362-1: Vials from tubular glass

- ISO 9001: Quality management
- ISO 15378: GMP Primary packaging
- 21 CFR 211 Subpart E – Control of Components and Drug Product Containers and Closures
- DMF type III
- Ph. Eur. USP and JP -> very complex!

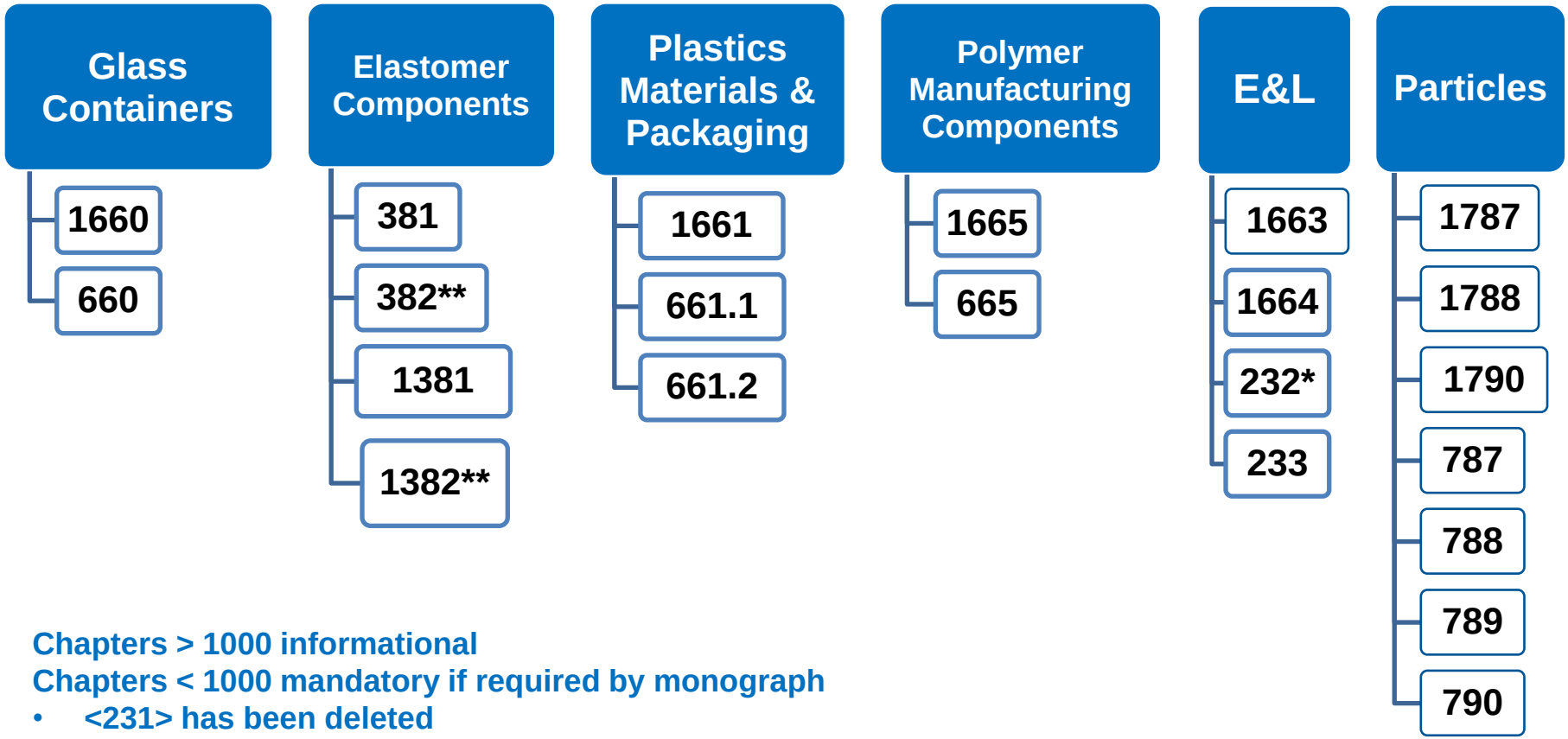
0.5 ml	47.6	6.85	4.65	1/2
1.0 ml long	54.0	8.15	6.35	1/2
1.0 ml standard	35.7	10.85	8.65	1/2 | 5/8
1.5 ml	43.2	10.85	8.65	1/2 | 5/8
2.25 ml	54.4	10.85	8.65	1/2

Global Pharmacopoeia



Overview of Relevant USP Chapters

USP
U.S. Pharmacopeia



Chapters > 1000 informational
Chapters < 1000 mandatory if required by monograph
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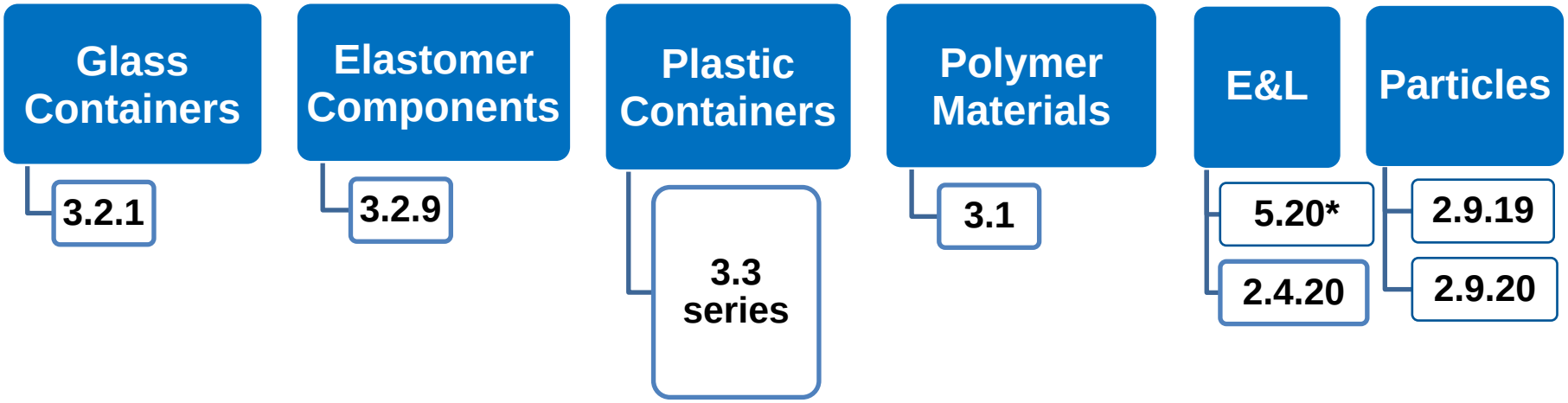
**** will be official 2025**

Overview of Relevant Ph Eur Chapters

European Pharmacopeia 10th Edition



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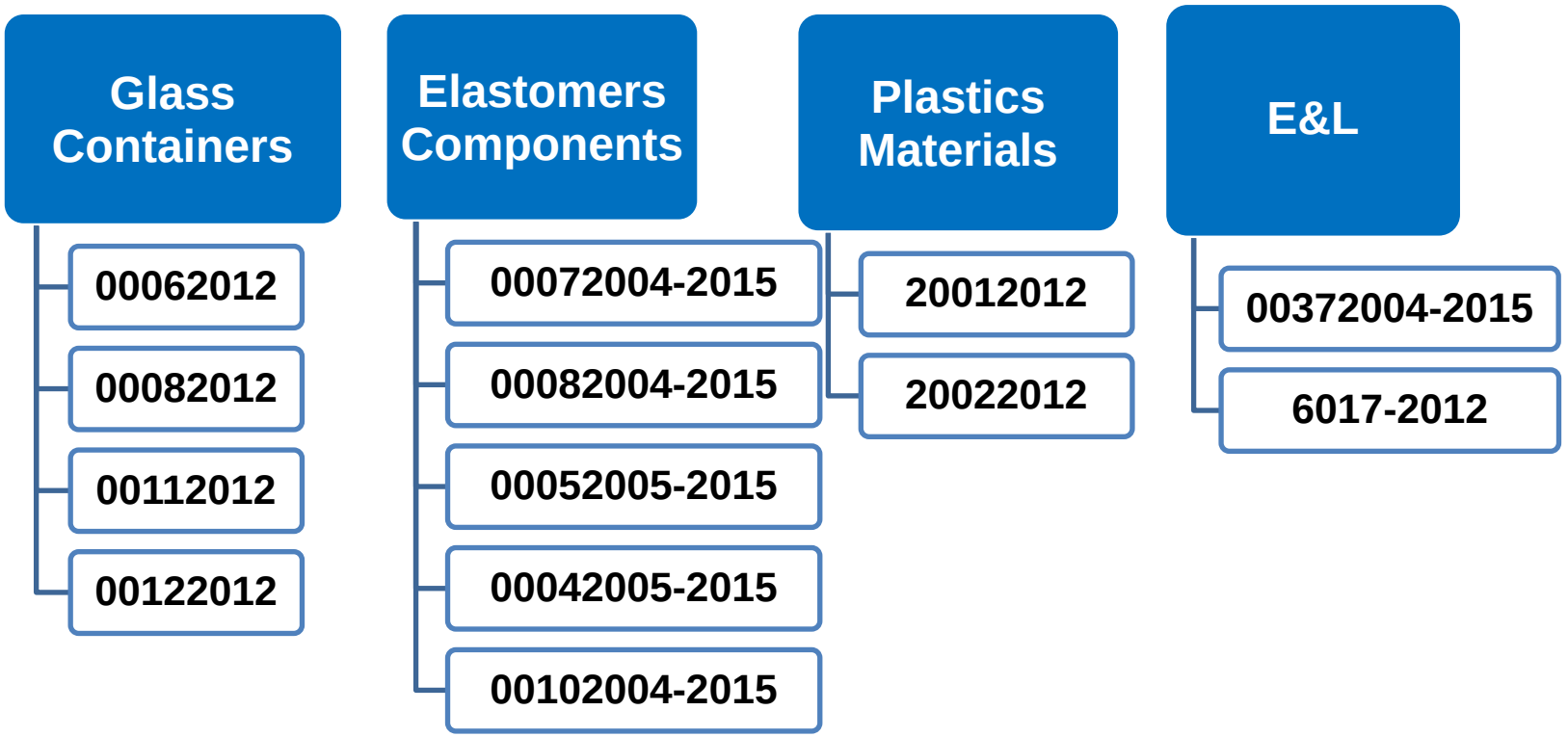
Overview of Relevant JP Chapters

JP
Japanese Pharmacopeia

Glass Containers	Elastomer Components	Plastic Materials	Polymer Manufacturing Components	E&L	Particles
7.01	7.03	7.02	-	1.07	6.07 6.08

Examples of Relevant YBB Standards

YBB



YBB standards are subsequently integrated into ChP for packaging material; 16 already became obsolete when ChP2020 became effective Dec 2020

Extract of Relevant ISO Standards

ISO

- **Glass Containers**
  - 719, 720
  - 4802-1, 4802-2
  - 11040-1, 11040-4, 11040-7
  - 8362-1, 8362-4
  - 13926-1
- **Elastomers Components**
  - 11040-2, 11040-3, 11040-5
  - 8362-2, 8362-3, 8362-5, 8362-6, 8362-7
  - 8871-2, 8871-4, 8871-5
  - 13926-3
- **Plastics Materials**
  - 11040-6, 11040-7
- **Polymer Manufacturing Components**
  - 9113
  - 17855
  - 2898
- **E&L**
  - 8871-1
- **Particles**
  - 8871-3

European Medical Device Directive vs. Medical Device Regulation

Before May 2021

Under Medical Device Directive (MDD)

- Immediate Packaging
- Application dossier: providing a summary of the product characteristics including the immediate and outer packaging as per 2001/83/EC, article 11, 6.4
- Self-certification for compliance of device functions to Essential Requirements in Medical Device Directive (93/42/EWG)

After May 2021

Under Medical Device Regulation (MDR)

- Article 1 (8) and (9): Definition of ”integral“
- Article 117: Application dossier for integral Drug Device Combination (DDC) has to contain the conformity assessment of the device part with the General Safety and Performance Requirements (**GSPRs**) (given in Annex I of MDR) issued by a notified body

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The Role of Notified Bodies and the European Medicines Agency

Notified Bodies

Assessing the

safety and performance

of **medical devices**

European Medicines Agency

Assessing the

quality, safety and efficacy of

medicinal products

Conformity Assessment

based on GSPRs is done by Notified Bodies (NBs)

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