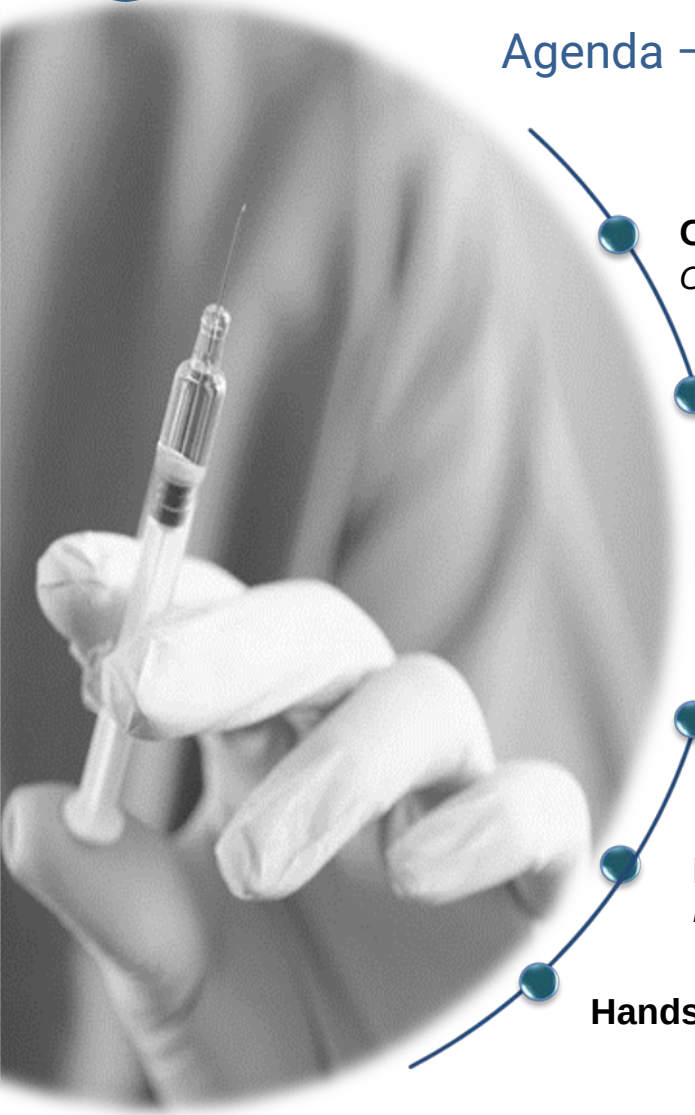
Agenda – DAY 1



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

Barrel forming

Glass cutting

Barrel forming

Printing

Cannula Assembly

Glass barrel production
Needle assembly, clean room class D (acc. GMP)

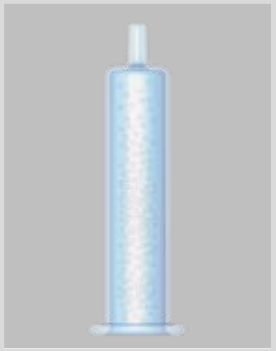
- 100 % in-process control (camera station for dimensions and cosmetic camera system)
- Quality control

Barrel forming Video

Needle Assembly Video

Washing and Siliconization

Washing (WFI)



Siliconization

Closure setting

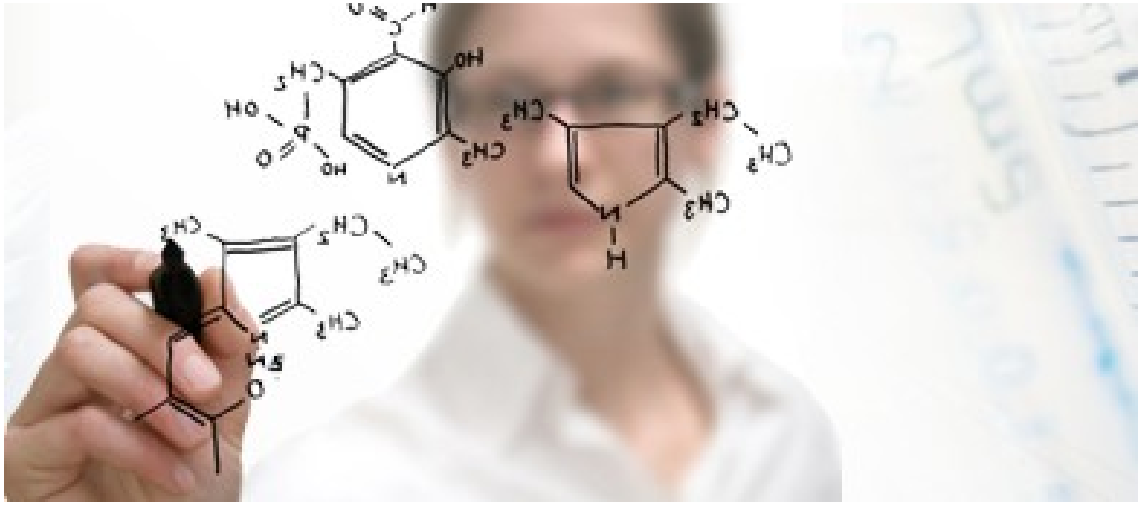
Nesting/coding
Packaging

RTF processing
Clean room ISO class 7 acc. class B under laminar flow

- 100 % in-process control
- Quality control

Washing and Siliconization Video

Sterilization



Sterilization by EtO treatment

- Pre-conditioning
- Desorption
- Final quality control
- Sterility testing
- Certificate of Conformity (CoC)

Regulatory Guidelines
for Prefillable Syringes

- ISO 9001: Quality management
- ISO 15378: GMP Primary packaging

  Primary packaging materials for medicinal products — Particular requirements for the application of ISO 9001:2015, with reference to good manufacturing practice (GMP)

- Containers and Closures are not defined in the cGMP regulations *but*
- **Interpreted** as the primary packaging of a finished drug product and treated acc. **21 CFR 211 Subpart E –** Control of Components and Drug Product Containers and Closures:

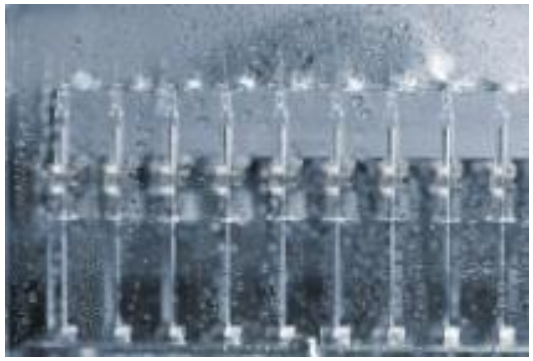
  glass, plastic or metal containers, bottles, vials, ampules, screw caps, lids, stoppers, seals, desiccants, fillers, etc.

- Products, methods procedures follow Ph. Eur. USP and JP
- Description of products, process and procedures in DMF type III
- Not covered with EU Medical Device Regulations, combination products regulations do not apply

Regulatory Guidelines
for Prefillable Syringes

21 CFR 211 Subpart E – Control of Components and Drug Product Containers and Closures

- Ensure compatibility/suitability of containers and closures
- Maintain inventory control
  - identification, storage, handling, sampling, testing
- Written and approved procedures
- Prevent contamination
  - Aseptic Processing CGMPs (high purity for rinse water)
  - Water system validation, USP <1231>
  - Water for Pharmaceutical Purposes
- Know suppliers and supply chain
- Appropriate sampling and testing



Regulatory Guidelines
for Prefillable Syringes

Combination Products/ EU Medical Device Regulation regulation not applicable
Prefillable syringe only becomes a combination product when filled

- ISO 10040-8 test procedures for filled PFS
- **21 CFR Part 4**
  - Combination product comprises two or more medical products
  - Co- development necessary, e.g. Biologic in a PFS in an AutoInjector
  - Mandatory steps: Design Control, Design History File, Risk Management, Design Verification, Validation, Usability studies

- Combination product development steps:
  - Drug characterization
  - Primary container selection
  - Manufacturing, labeling, logistics…

This workshop!
Vendors can help, but
don´t have all the data

- FDA Guidance - Current Good Manufacturing Practice - Requirements for Combination Products

Define and select primary packaging container early in development: *the syringe brings the drug into the patient*

Hands-on Session 1

- Prefilled syringes
- Test break loose and gliding force, “just inject”
- Safety devices