

# Technical considerations on test sets for difficult to inspect products

CONNECTING  
PEOPLE  
SCIENCE AND  
REGULATION®



PDA  
TRAINING

# Difficult to inspect products

- A difficult to inspect product for parenteral use is a product
  - „Where the nature of the contents or the container-closure system permits only limited capability for inspection of the total contents“ – USP <790>
  - „Product/container combinations that obscure particulates are commonly known as „difficult-to-inspect“ parenterals“ – PDA TR79



# Difficult to inspect products

- Challenges from the laboratory perspective:
  - Preparation of defect samples oftentimes problematic
  - Aspects that are proven to be working for the sample preparation of one container form/for one product might be unusable for other projects

Figuring out the optimal way to prepare different defects and the best ways to avoid unnecessary problems during the usage of the test kit is a matter of experience

# DiP – Large volume containers



Large volume:

- Containers with a filling volume of >100ml
- Most often molded glass containers or Infusion bags

Problems:

- Surface area is much larger
- Infusion bags often made out of flexible opaque plastics with print
- Verification of only one particle challenging
- Molded glass thickness differs a lot in one container

# DiP – Small volume containers

Small volume:

- Containers with a filling volume of <math><1\text{ml}</math>

Problems during preparation:

- Particles are difficult to get in solution
- Surface area is very small -> tendency of particles to stick to the container wall
- Low filling volume makes it difficult to get particles in motion



# DiP - Lyo Containers

- Lyo cake characteristics
  - Mostly white appearance
  - Sometimes loose and movable in the container
  - Often unstable product
  - Breakage of lyo cake
  - Dusty powder at glass wall



-> preparation of Lyo standard samples is very challenging

# DiP - Lyo Containers

Problem 1:

Lyo cake is mostly white and not transparent



- Particles locations

- Bottom or sidewall

Possible to detect by eye

- Surface

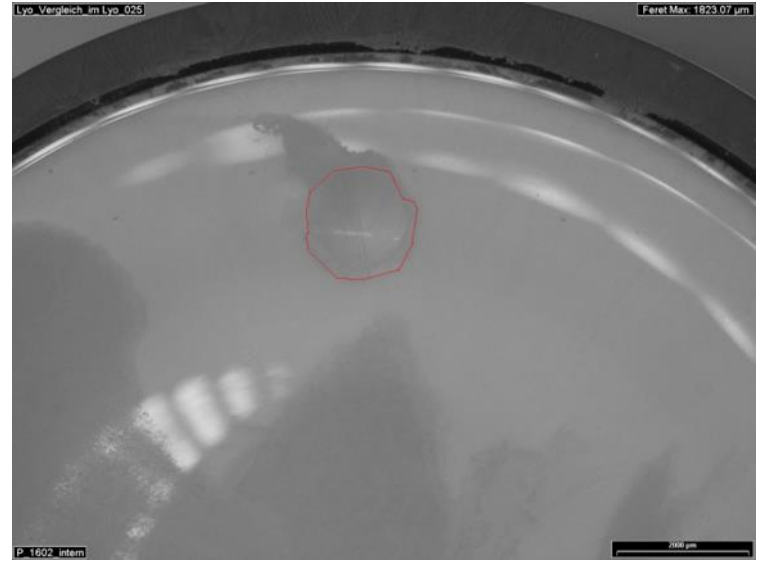
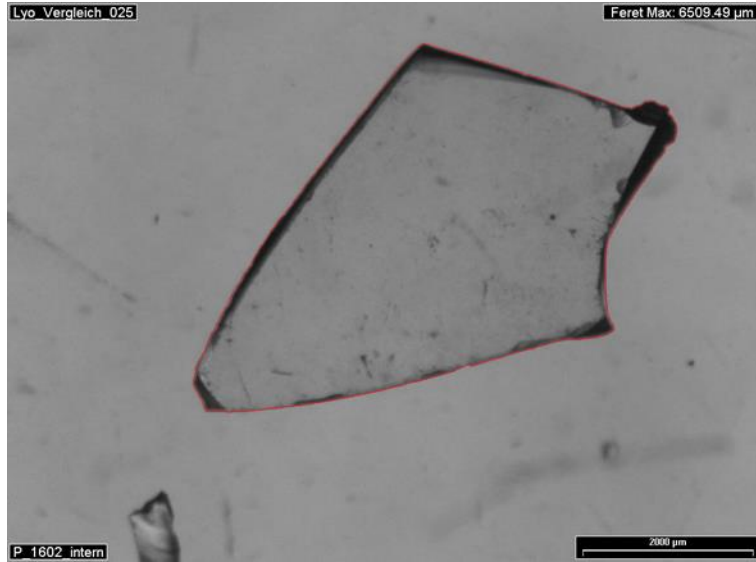
Possible to detect by eye

- Inside of lyo cake

**Impossible to detect by eye**

Solution: Fixing of particles to the surface, sidewall or bottom of the container

# Loose glass particle





# DiP - Lyo Containers

Problem 2:

Lyo cake is unstable

- Detachment of the lyo cake
- Breakage of the Lyo cake
- White powder on the glass wall

➤ Test sets with original product are not usable multiple times



# DiP - Lyo Containers

Solution: Development of an additive that stabilizes the Lyo cake

- Long time stability
- No interaction with the solution
- No discoloration
- Appearance close to the original Lyo product



# DiP – Infusion bags

Plastic flexible bags combine different factors that make them difficult to inspect:

- Often large volume containers
- Often preprinted
- Container oftentimes opaque
- Might have additional tubing, ports or multiple chambers



# DiP – Infusion bags

Problems during preparation:

- How to insert the particles into the container?
  - Different methods need to be tested for each unique Infusion bag.
  - Oftentimes preparation through the tubing is the most practical
- Electrostatic attraction
  - Flaming of the canula or using a deionizer
- Tubing oftentimes opaque



# DiP – Solutions with turbidity or colour

Turbid products or deeply coloured products can make the visual inspection process very difficult

- Problems during preparation process:
  - When using a placebo solution, the physical properties should be maintained while increasing the shelf life
  - Qualification and methods to prepare the placebo solutions must be tested -> long term stability
  - Detection of particles is difficult



# BFS-containers

- Problem:
  - Transparency and thickness
  - Transfer of particles inside the container
  - Fragility of the container format
  - Particles tend to stick to the polymere of the container



# BFS-containers

- Solution
  - Particles with **high contrast** to enhance visibility and detection rate
  - Particles having a larger size limit tend to not stick to the container as much



# DiP – Coloured/amber containers

- Particle selection differs from „normal“ transparent containers
  - E.g. white fiber/glass particles difficult to find
- Cosmetic defect detection is also challenging
  - E.g. Discoloration -> Adjustment of the colour oftentimes necessary





# DiP – Solutions with high viscosity

- Difficult to get particles in solution
  - Difficult to find particles via rotation
  - Filling of containers with the highly viscous solution might be a problem
- } Particles oftentimes float on the surface

CONNECTING  
PEOPLE  
SCIENCE AND  
REGULATION®



PDA  
TRAINING

[pda.org](http://pda.org)