Challenges from a laboratory perspective

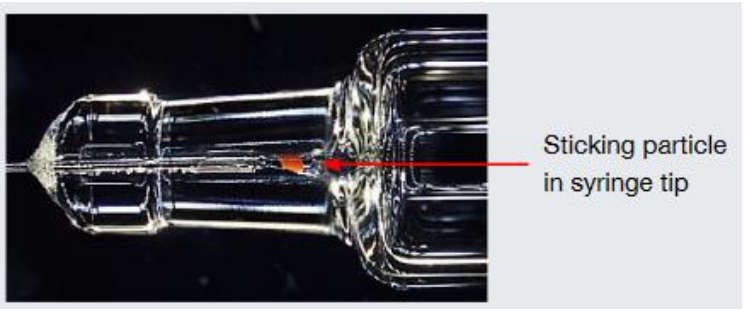
PDA Parenteral Drug Association

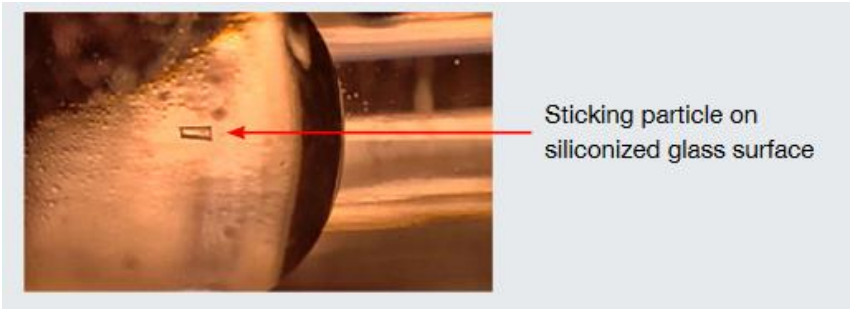
PDA TRAINING

Sticky particles

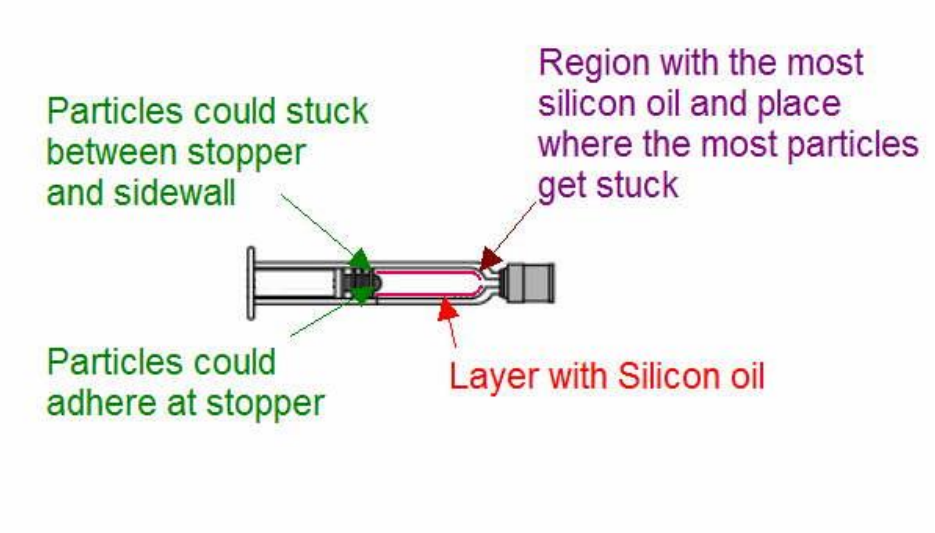
Problem:

- Prepared particles tend to stick to the container or the closure, especially to siliconized surfaces
- Differences between different particle sources and sizes





Sticky particles



Sticky particles

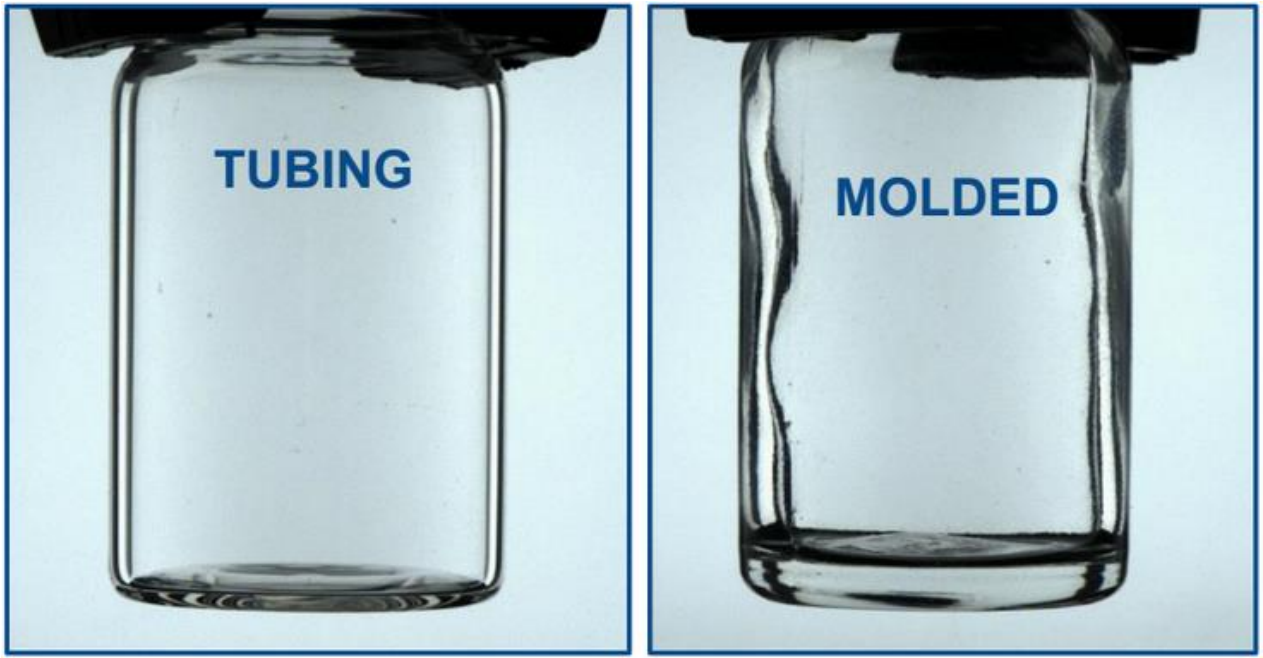
Solution:

– Desiliconize the containers with an appropriate solvent
  - Behaviour must be checked to see if the product behaves differently in a container without silicon layer

– Usage of particles with a specific form factor to reduce the risk
  - Need of quite some data to confirm which particles sources and form factors have the highest chance of not sticking

– Closing of the canula to prevent particles from getting lost

Molded and tubular glass defects



Molded and tubular glass defects

- Problem:
  - Preparation methods differ when creating glass defects in molded and tubular glass containers
  - Molded glass has a much more unpredictable behaviour due to the structural composition of the container
  - When setting up SOPs for the preparation of glass defects it is not possible to adopt procedures without testing them
  - Inspection of molded glass containers more difficult because of the uneven thickness of the glass
  - Molded containers oftentimes already have inclusions or airlines

Molded and tubular glass defects

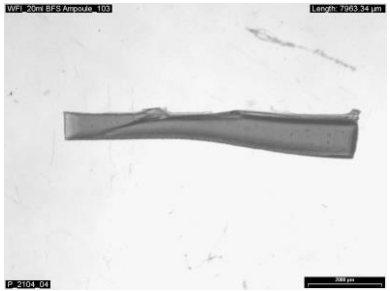
- Practical tips:
  - Procedures for the preparation of glass defects have to be tested for each container family
  - New procedures have to be developed if the trusted methods won‘t work for a new container format
  - Especially larger volume molded containers will behave unpredictably
    - Usage of particles with a higher contrast or larger particles due to enhanced PoD

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



Highly viscous products

Problems:

- A highly viscous solution makes it difficult for the particles to get into solution
- Particles, once inserted, are behaving nearly static
- Air bubbles take a long time to rise and dissolve
- Filling of solution harder
- If a placebo solution is used a thickener should be used that combines long term stability and similiar appearence to the original product

Highly viscous products

Practical tips:

– The behaviour of different particle sources in a highly viscous product should be tested beforehand

– Feret max is not the only interesting parameter in this case, form factor and weight of the particle

– Using the sidewall to paste the particle in the container makes the final inspection much easier

Toxic products

Problem:

– Preparation of a toxic original product must follow strict rules and needs specially trained preparators

– Most external and internal laboratories are not equipped for the task

-> the use of a placebo solution is nearly always the right decision

Foaming products

Problem:

– During particle preparation smaller particle sizes tend to float on the foam

-> risk of particles sticking to the stopper

– Foaming of a product also makes the inspection of the containers after preparation harder, especially in highly viscous solutions

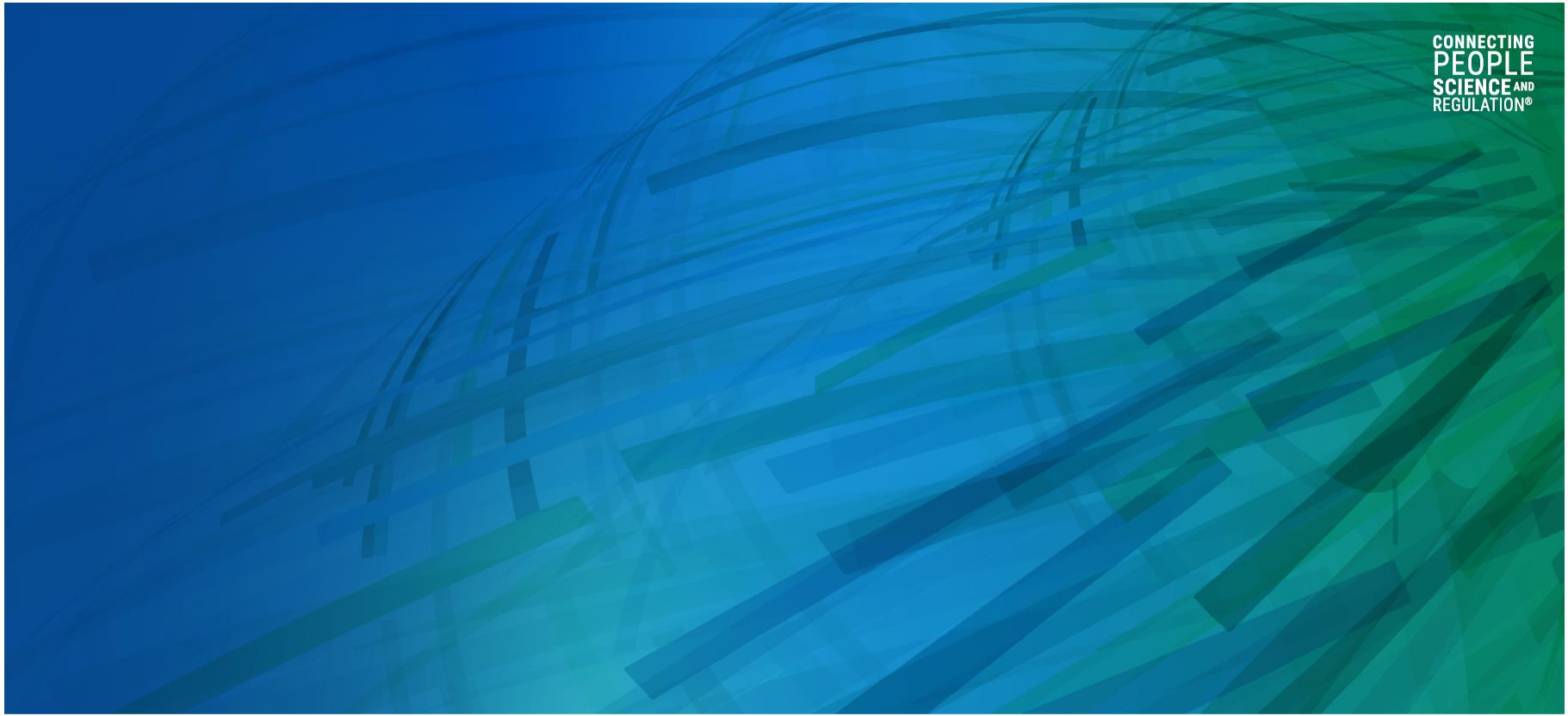
-> Prepared samples need to stay still for a while to ensure that the foam dissolves

Air bubbles in product

- Problem:
  - Air bubbles make it difficult to find certain kinds of particles inside a solution (e.g. glass particles)
  - Air bubbles remain stable in highly viscous solutions for a long time

    -> some cooldown time is required before the final inspection
  - Air bubbles are easiliy confused with e.g. glass particles

    -> operators need special training to differentiate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