
PDA
Parenteral Drug Association

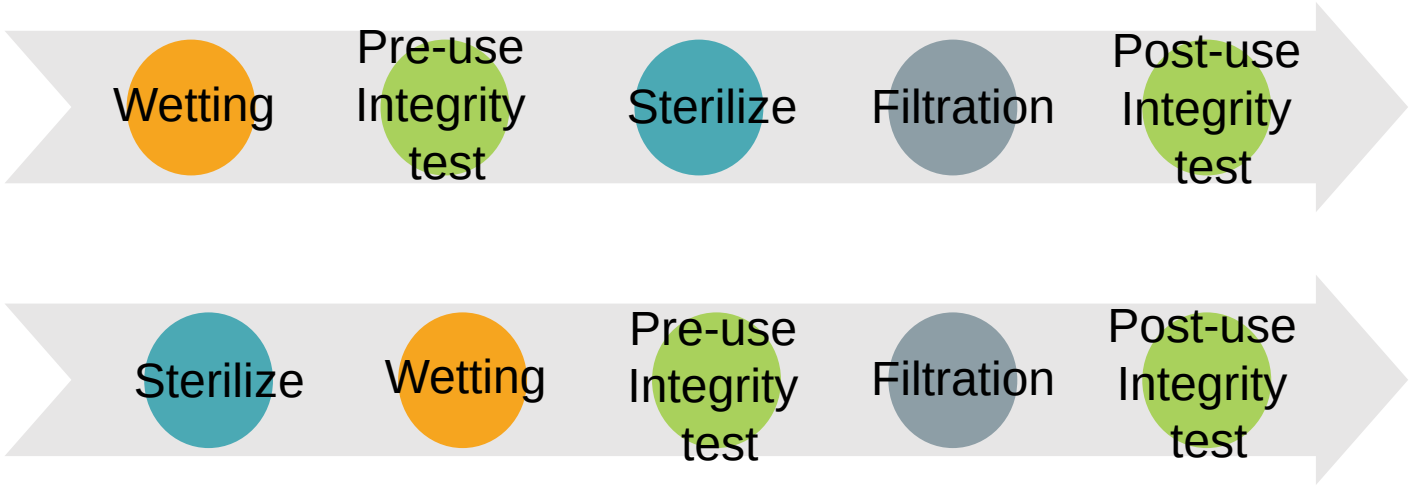

BioPhorum

PUPSIT
Practical implications and decision making

Presenter
Steve Ensign
Sr Consultant Engineer
Eli Lilly and Company

What is PUPSIT?

- IT performed **pre-use** to confirm that filter starts out integral
- IT performed **post-use** to confirm that filter remained integral during filtration operation
- The details around the timing of the “pre-use” IT determines whether or not PUPSIT compliant
  - Common within industry to perform pre-use integrity testing **prior to sterilization** (particularly if sterilization method was not SIP).
- These changes may cause changes to the filtration process

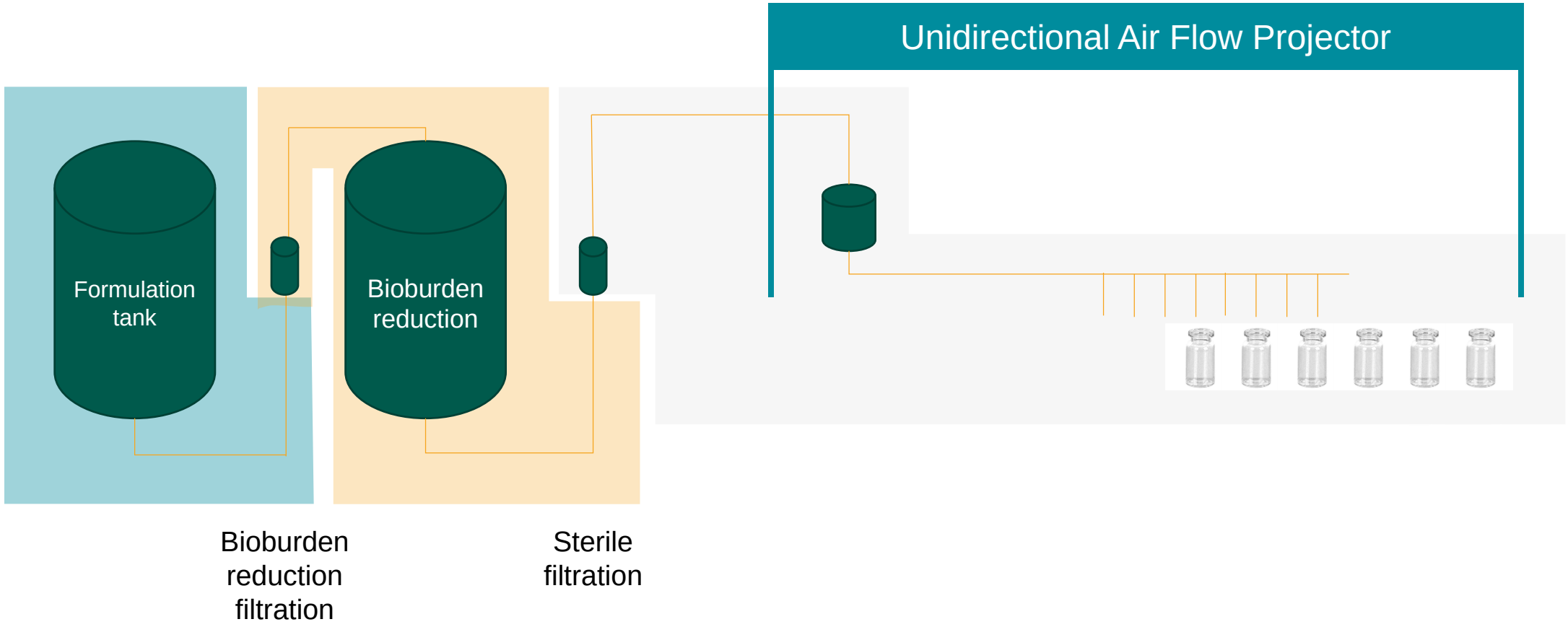


PUPSIT – practical implications and decision making

Goal

Using a representative example, review a theoretical case study in PUPSIT implementation and the points to consider in getting there

Example process – formulation and filling

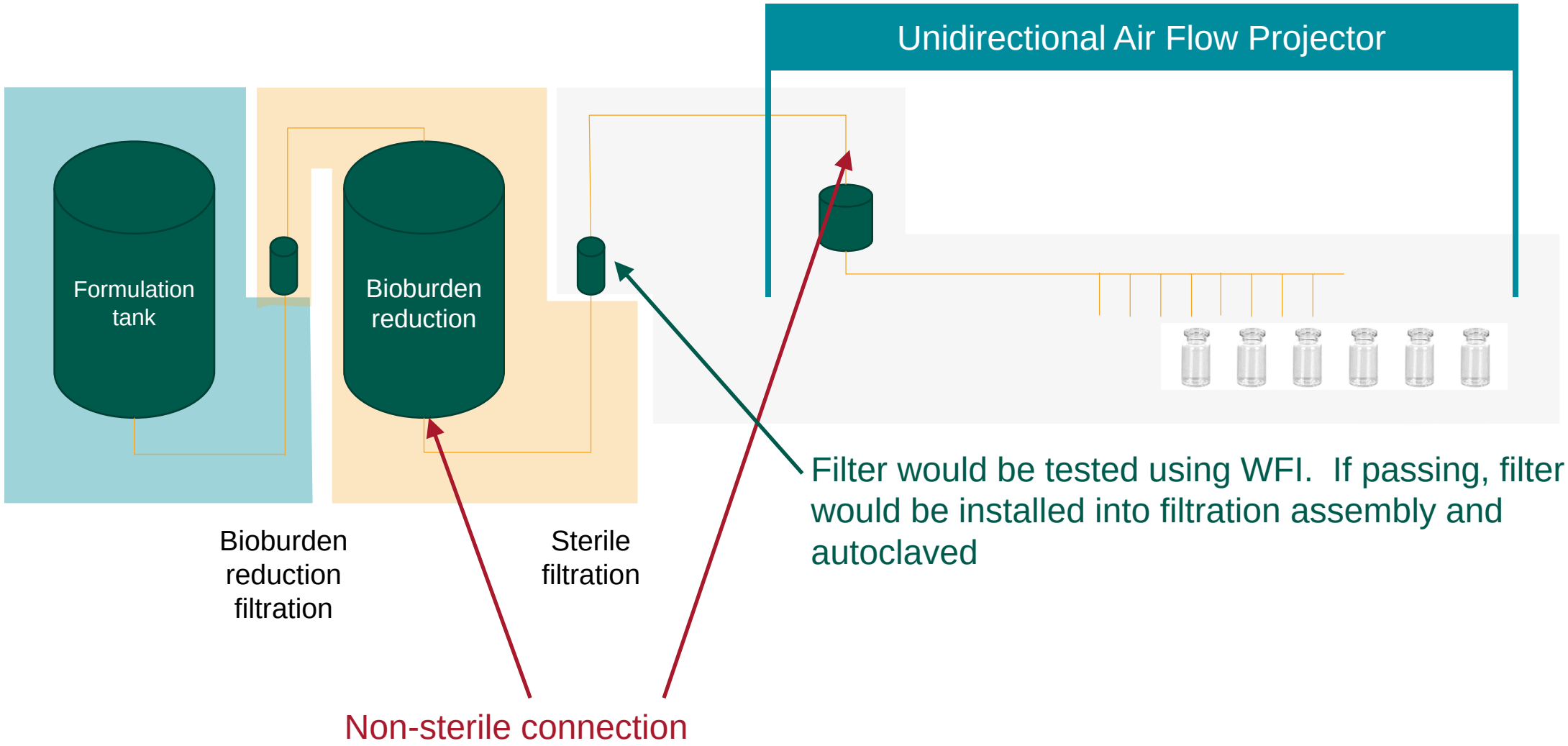


Somewhat typical sterile filtration process

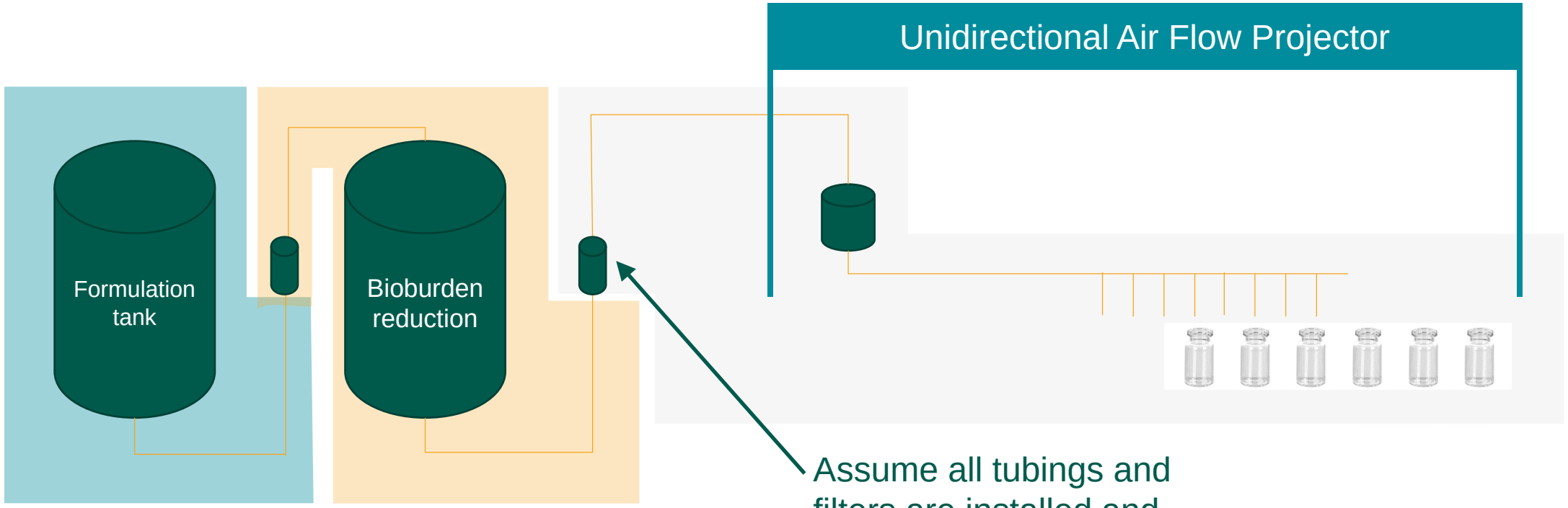
Typical steps for PUPSIT

- Wetting the filter membrane and venting displaced air
- Performing the integrity test of the sterilizing grade filter
- If necessary, performing an air blow to dry the filter assembly
- If necessary, re-wet the filter for filtration
- If necessary, diverting of initial process fluid for discard
- Performing the integrity test of any vent filters associated with PUPSIT

Historical filter testing process



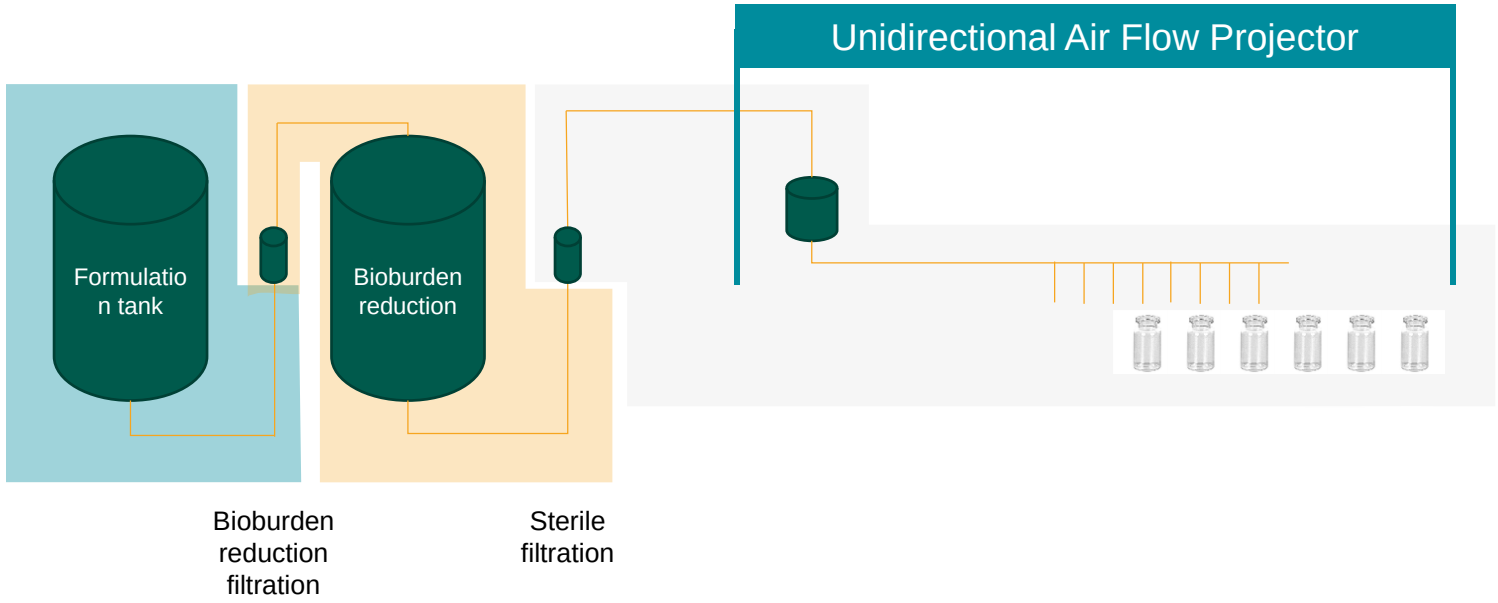
Change to a PUPSIT compliant process



Discussion points

- Integrity Testing
  - Wetting fluid
  - Downstream venting/back pressure
  - Test type
  - Tubing selection
  - Redundant filtration
  - Temperature considerations
- Risks to maintaining sterility
- Change Control considerations
- Typical Steps for PUPSIT

Integrity Test – wetting fluid

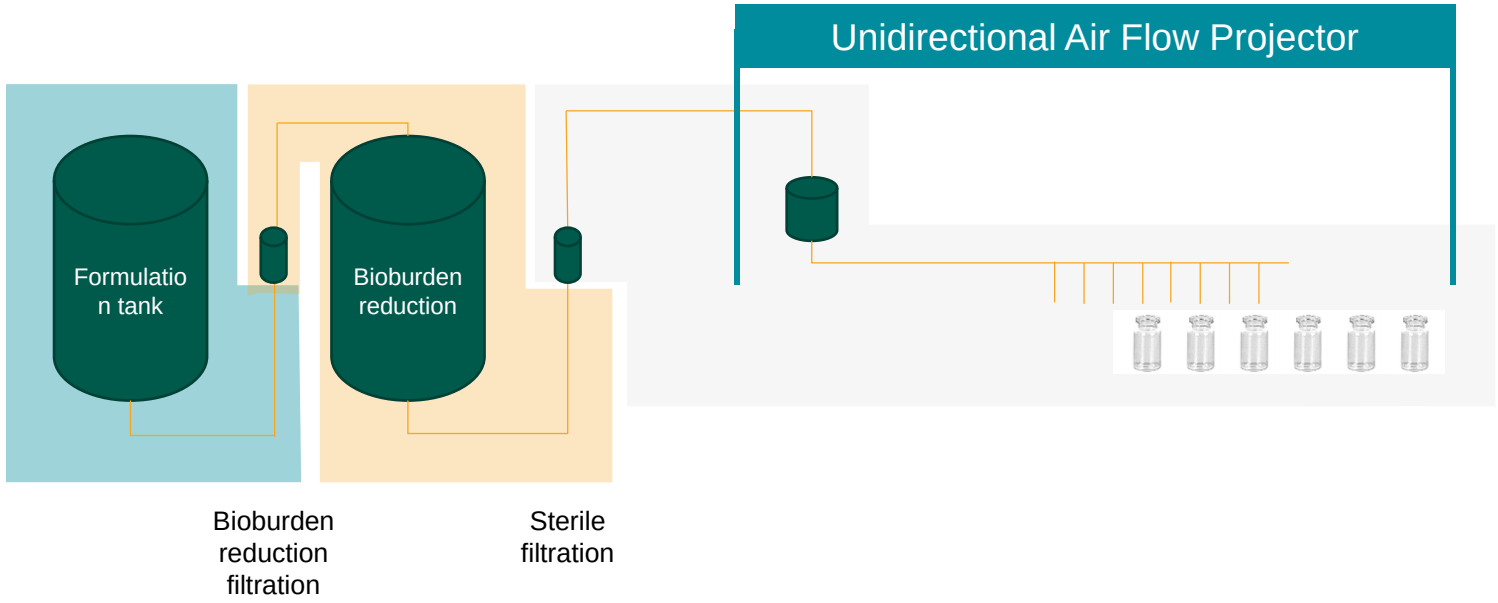


- Typical choices are product, water, buffer but there are others
- Water is known; buffer/product may not be (discuss temperature later)

Questions

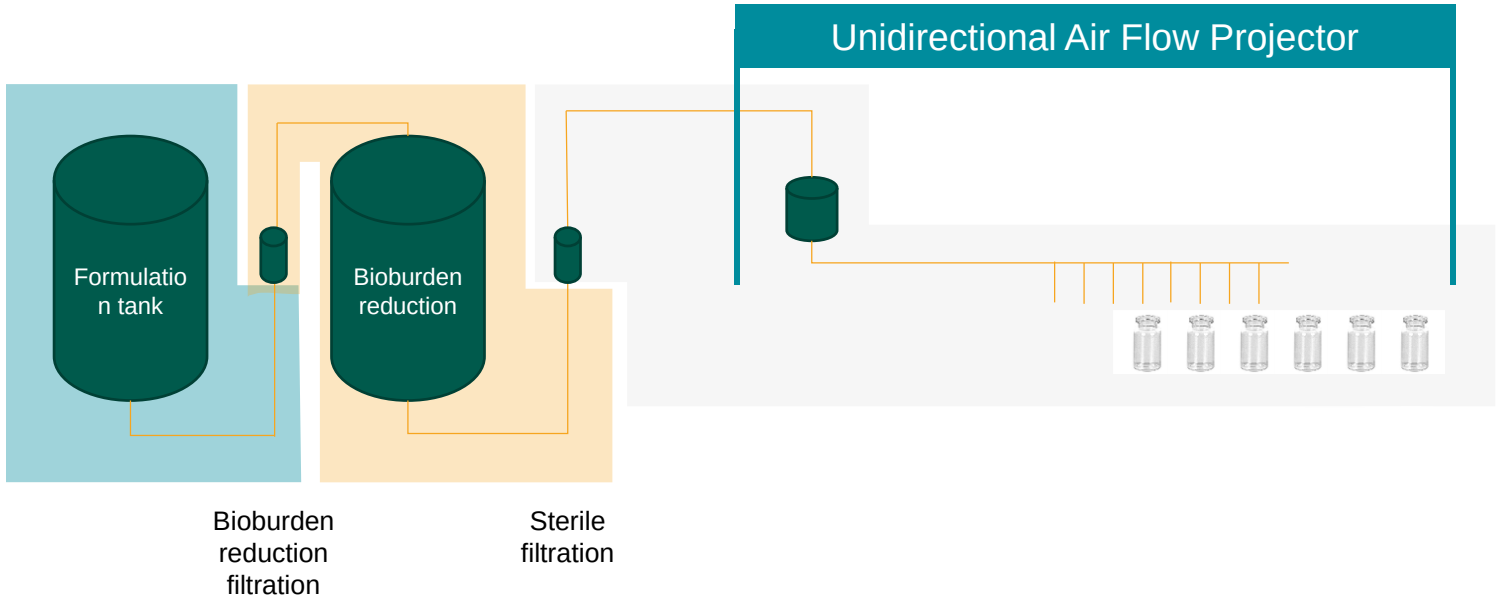
- Can product take pressures of integrity testing?
- How to manage dilution effect of water/buffer
- Where will wetting flow and test effluent be collected?
- Availability/cost of product
- Wetting fluid that is not well defined can lead to changing results.
- Is a blowdown needed following the integrity test

Integrity test – downstream venting / back pressure



- Downstream of filter, pressure should be atmospheric or will have an impact on the integrity test result
  - High downstream pressure could increase integrity test result artificially.

Integrity test – test type

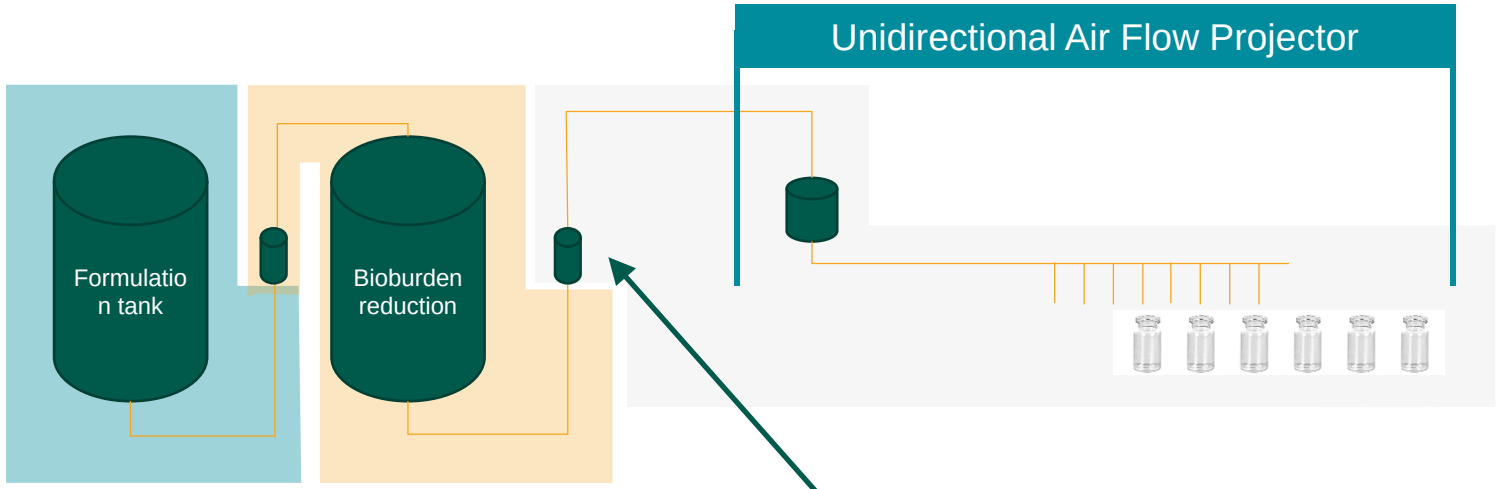


- Common tests are bubble point, diffusion / forward flow
  - Diffusion is performed at lower pressure than BP (tubing discussion next slide)

Questions

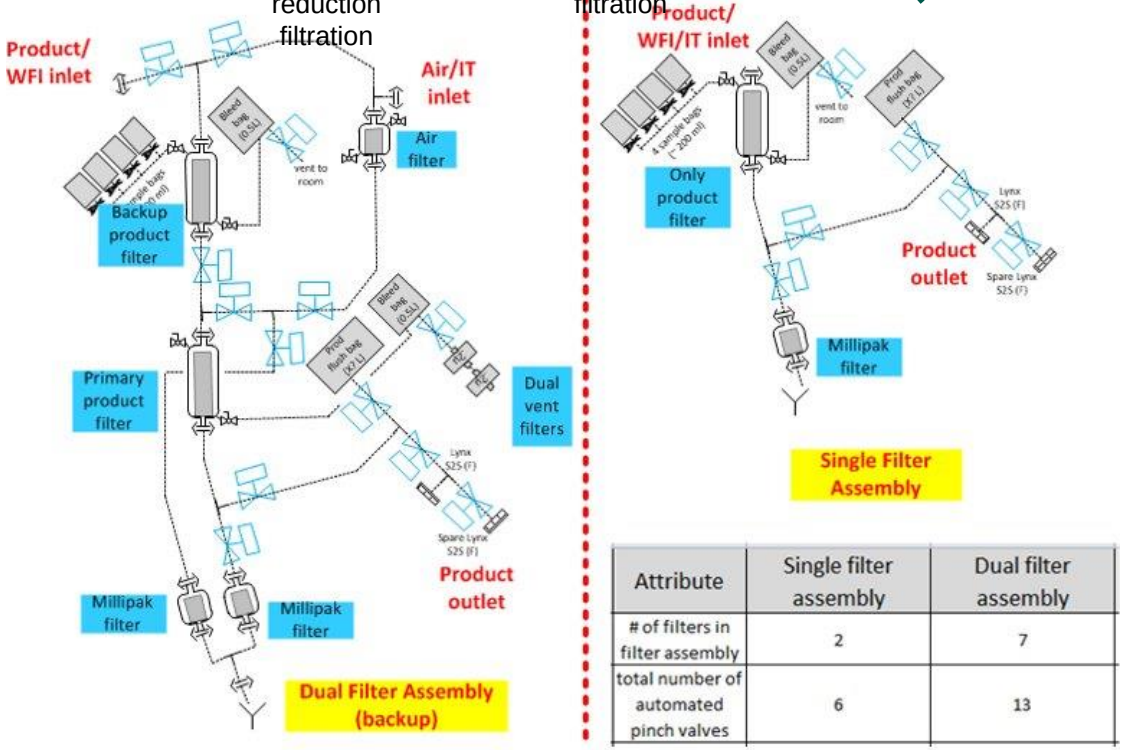
- Is data known for given test type?
- Some tests require fuller wetting due to higher pressures used

Integrity test – redundant filtration



Bioburden reduction filtration

Sterile filtration

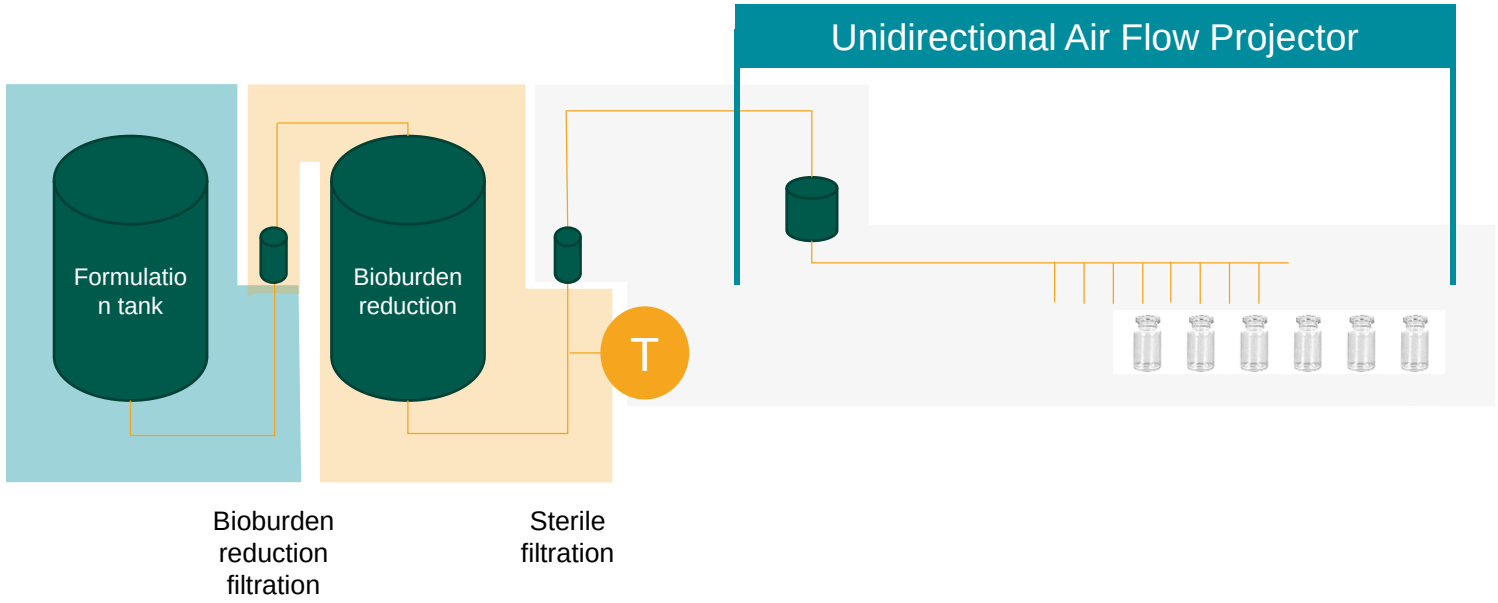


Attribute	Single filter assembly	Dual filter assembly
# of filters in filter assembly	2	7
total number of automated pinch valves	6	13

- Redundant filtration great complicates PUPSIT
- It adds to number of connections, valves and filters and many are within the sterile boundary (past first product filter)

2 filters vs 7; 6 valves vs 13

Integrity test – temperature considerations

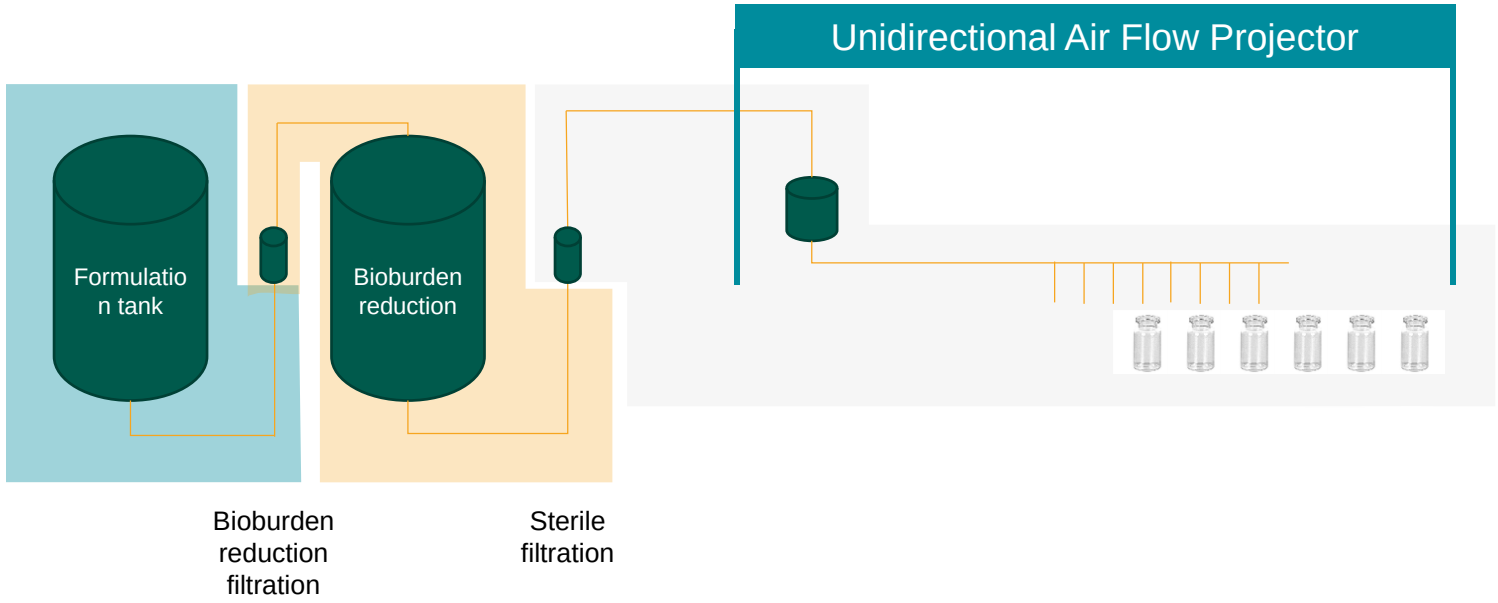


- Testing pre-PUPSIT, WFI temp to filter was easy to control
- May know product characteristics at room temperature
- Unless otherwise specified, fluid characterization tests are run at 22C +/- 4C

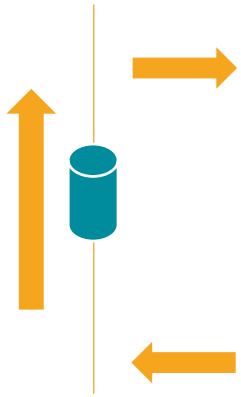
Question

- What is temperature of product during wetting phase?
- Does your test cover this temperature?

Risks to maintaining sterility



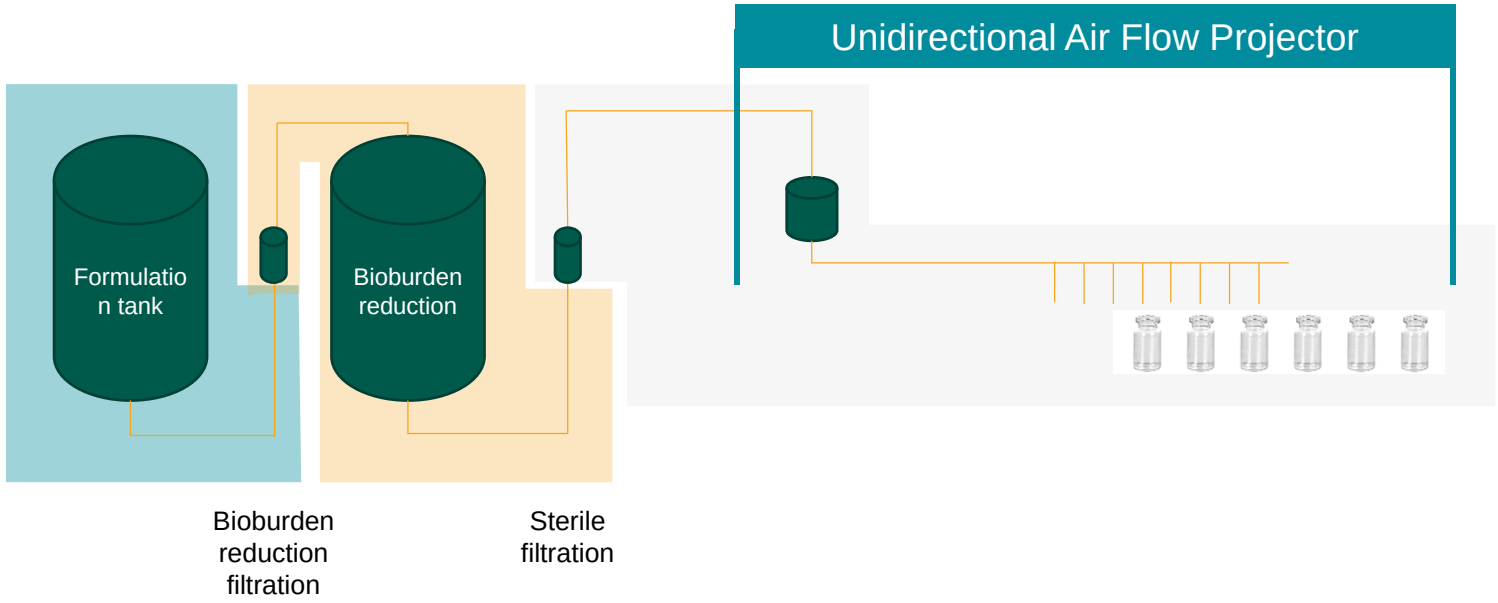
- Minimize manual manipulation of valves within sterile boundary (were not previously needed)
- Minimize number of connections after sterile filter
- Maintain positive pressure or protected by Grade A airflow



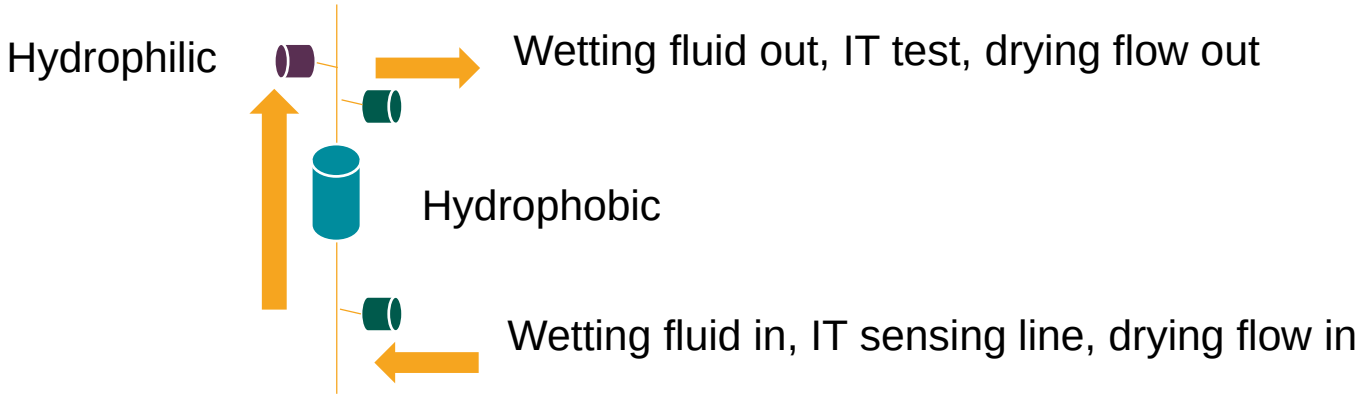
Wetting fluid out, IT test, drying flow out

Wetting fluid in, IT sensing line, drying flow in

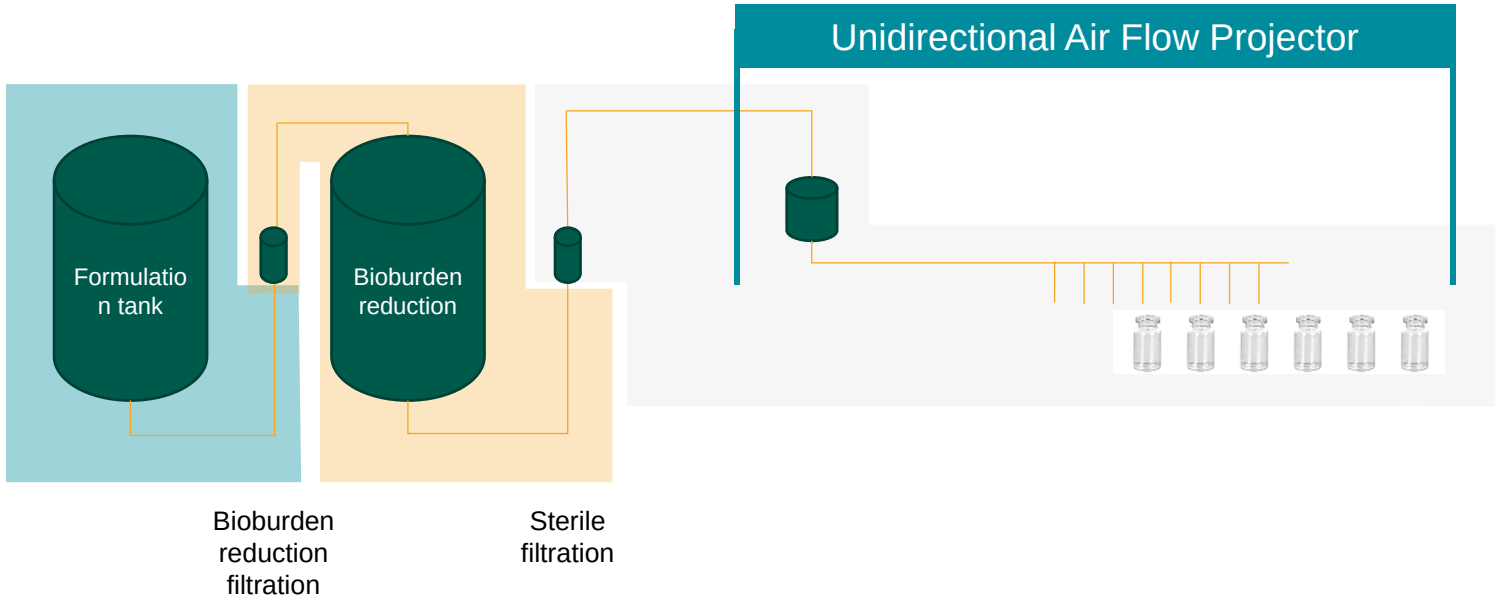
Risks to maintaining sterility



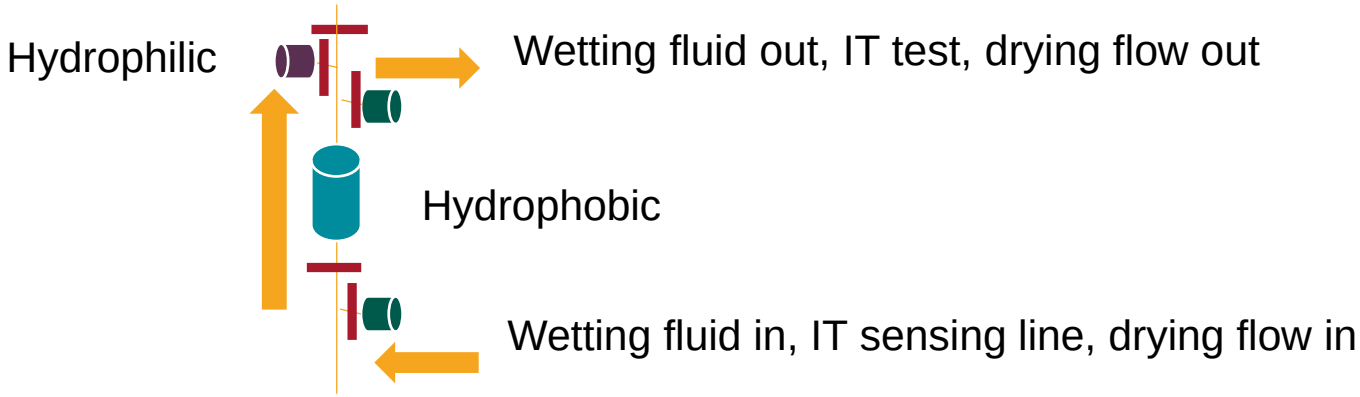
- Adding in filters to support flow paths



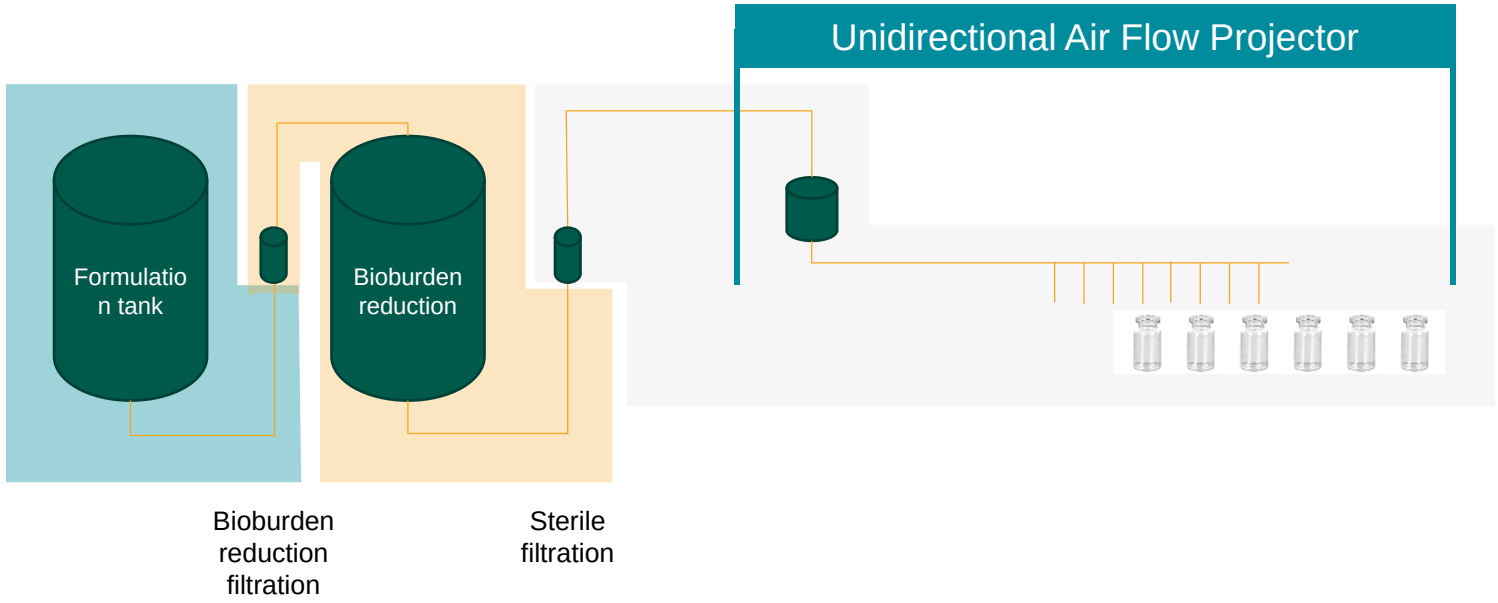
Risks to maintaining sterility



- Adding in valves/tubing pinches to support flow paths

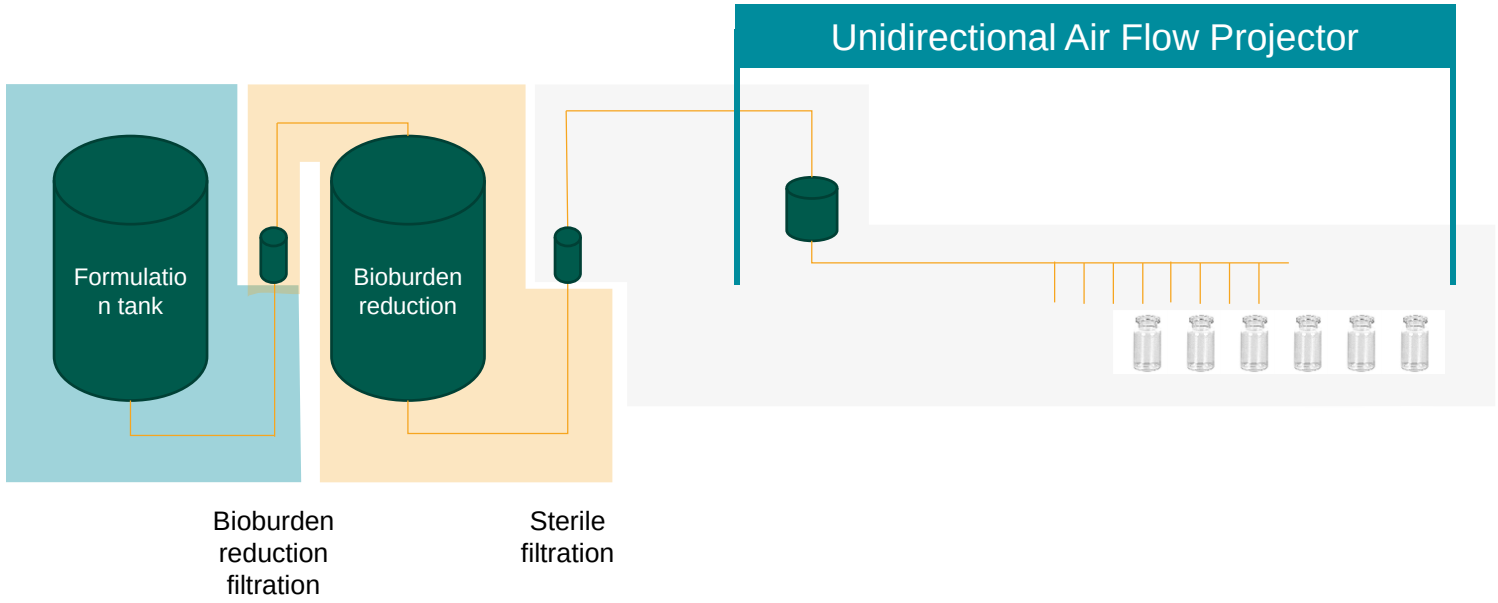


Some change control considerations



- New equipment/automation
- SOPs/Training
- Impact on consumable items
- Impact on registrations
- Etc.

Integrity test – tubing selection



- Pre-PUPSIT, tubing may only see ~ 1-1.5 bar
- PUPSIT tubing upstream of filter can see ~ 3.5 bar
- Beware of tubing leaks

Final notes

- There are many process designs and variations that should be taken into account when designing and performing PUPSIT properly and safely.
- Collective experience has shown that where PUPSIT assemblies are not designed properly or PUPSIT procedures are not performed correctly, the sterility of the final product is put at risk.
- Any procedure performed during an aseptic process and on the downstream side of the sterilized system an be inherently risky and must be properly controlled.

Thank you

Any questions?