Sterility Maintenance in Aseptic Systems

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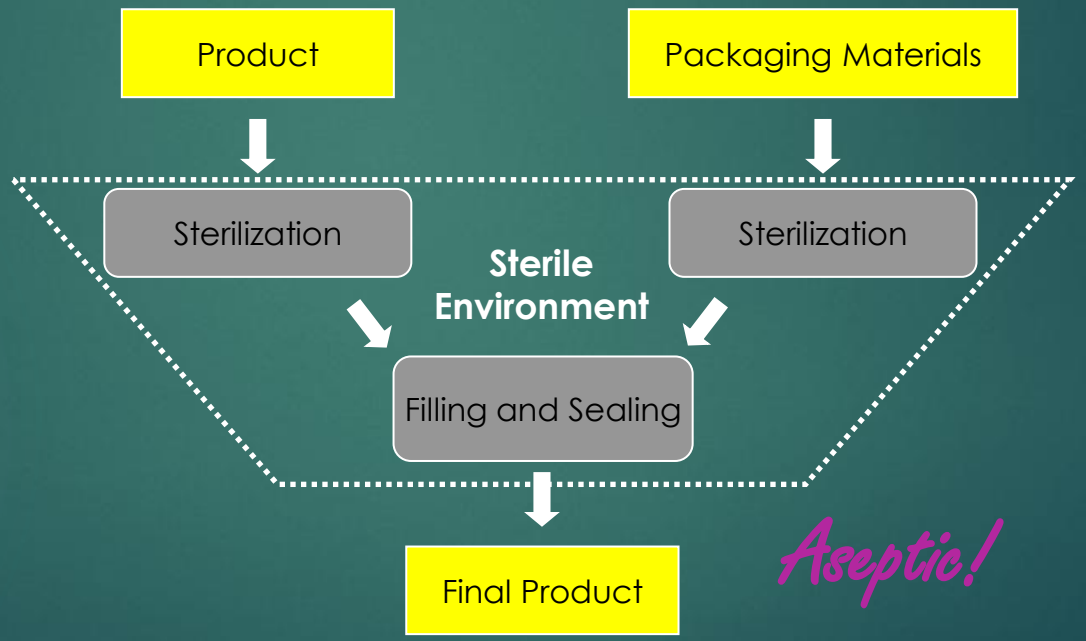
The views expressed in this presentation are those of the authors and do not necessarily reflect the position or policy of PepsiCo and WhiteWave

Dave's Not Here

Aseptic Systems

- Achieve and Maintain sterility for the product, package and the sterile zone



Aseptic System Failures

- Rarely (if ever) a failure to sterilize the product, package or clean equipment in the sterile zone
- Yet this is where the bulk of the validation efforts lie

Geissler and Boenigk, An overview of Root Causes and Troubleshooting Procedures for Spoilage Diagnosis, IFTPS 2012

Aseptic Systems Guidance

- Available for validation of achieving sterility particularly for product and package (IFTPS, FDA, EHEDG, VDMA, CODEX)
- Not so much for system design and sterility maintenance

VDMA

X ALIMENTARIUS

FDA

IFTPS

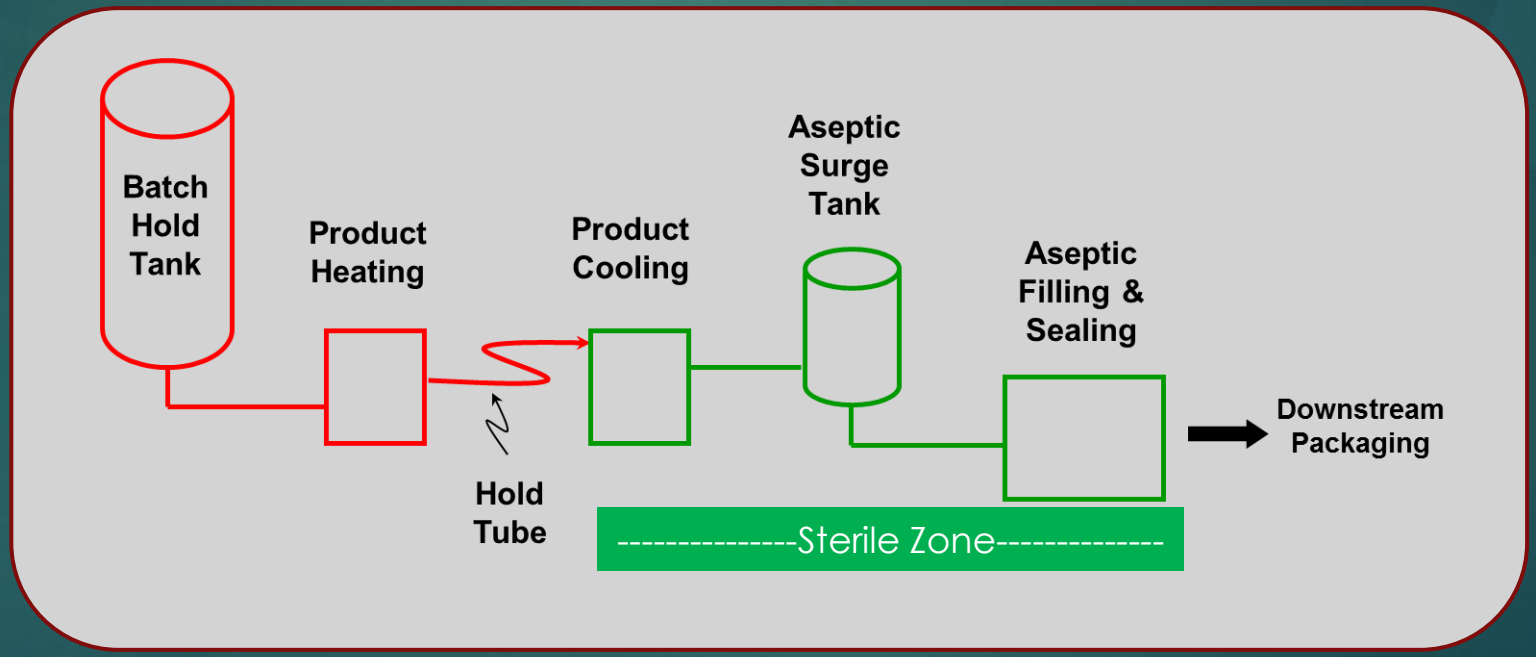
EHEDG
EUROPEAN HYGIENIC EQUIPMENT DESIGN GROUP

Sterility Maintenance

- This talk does not address the sterility parameters that are associated with the validation of achieving sterility (e.g., product time and temperature in the hold tube, steriliant concentration and temperature)
- Rather this discussion is around the other factors that help maintain sterility in an aseptic system, some of which may not be part of a process filing.

Sterile Zone

- All the equipment after the end of the hold tube up to the point where the product is sealed in the package.



Methods of Sterility Maintenance

- System Design
- Sterile Barriers
- Differential Pressure
- Avoid Risky Behaviors

System Design

- Keep it simple –not like this
- Choose equipment designed for use in aseptic systems
- Place cold spots and sterile barriers in appropriate locations
- Consider transitional phases

Aseptic Equipment

- Sanitary equipment that also is designed to:
  - Keep nonsterile components out of sterile zone,
  - Have appropriate barriers implemented, and
  - Have the tolerance to withstand the sterilization conditions

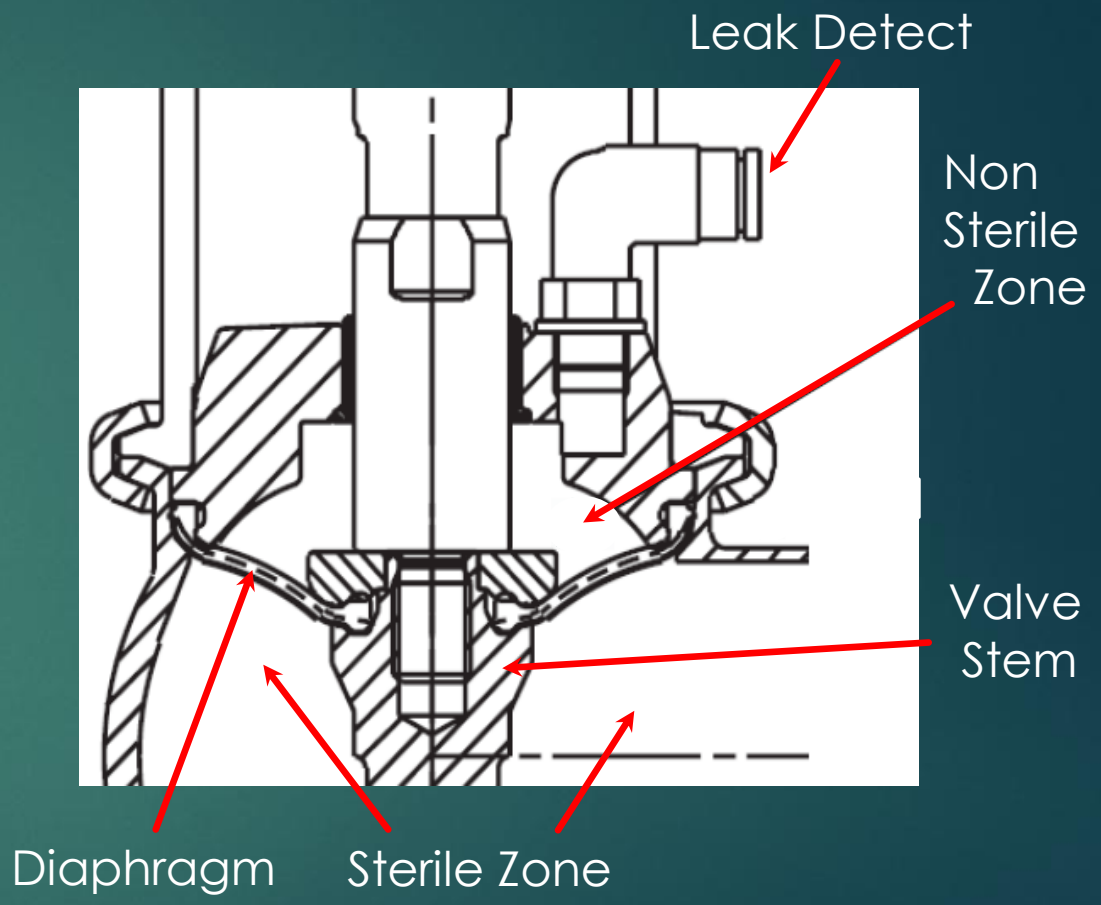
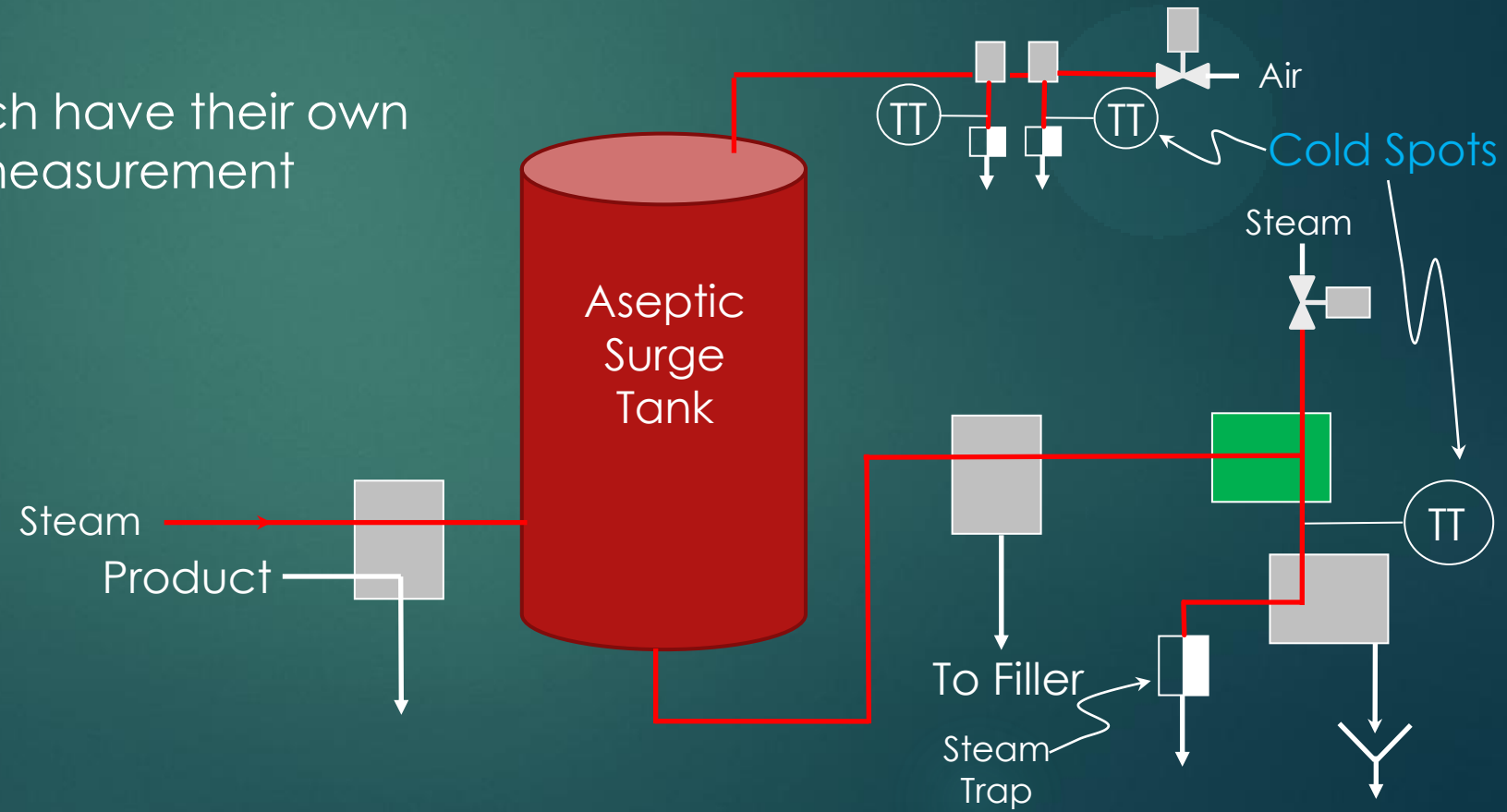


Diagram Courtesy of Tetra Pak

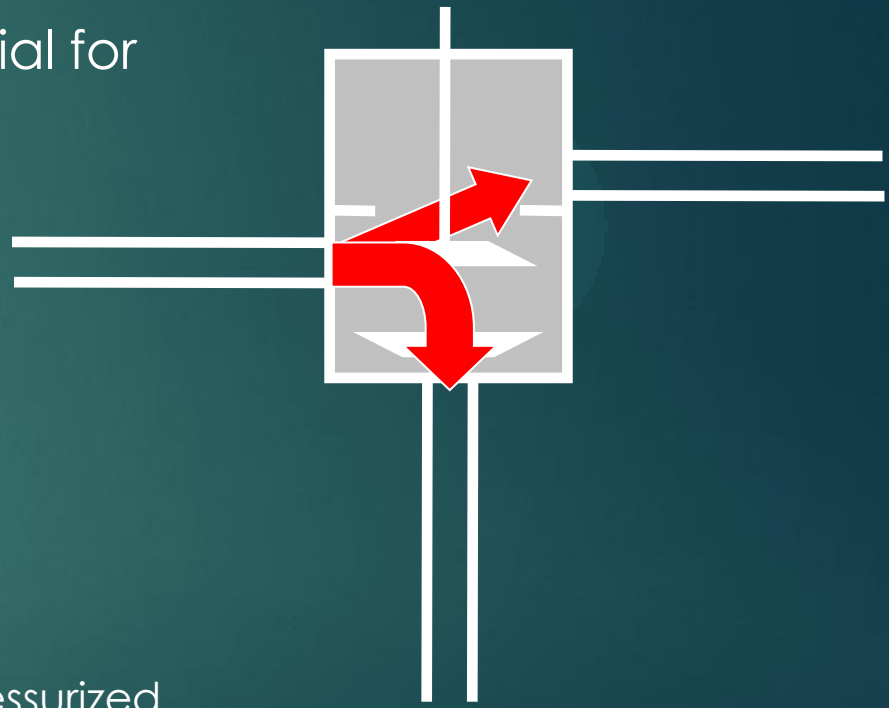
Cold Spots

- Point were temperature is measured to show that the entire line or part of the line is achieving the proper sterilization conditions
- Parallel paths should each have their own cold spot temperature measurement



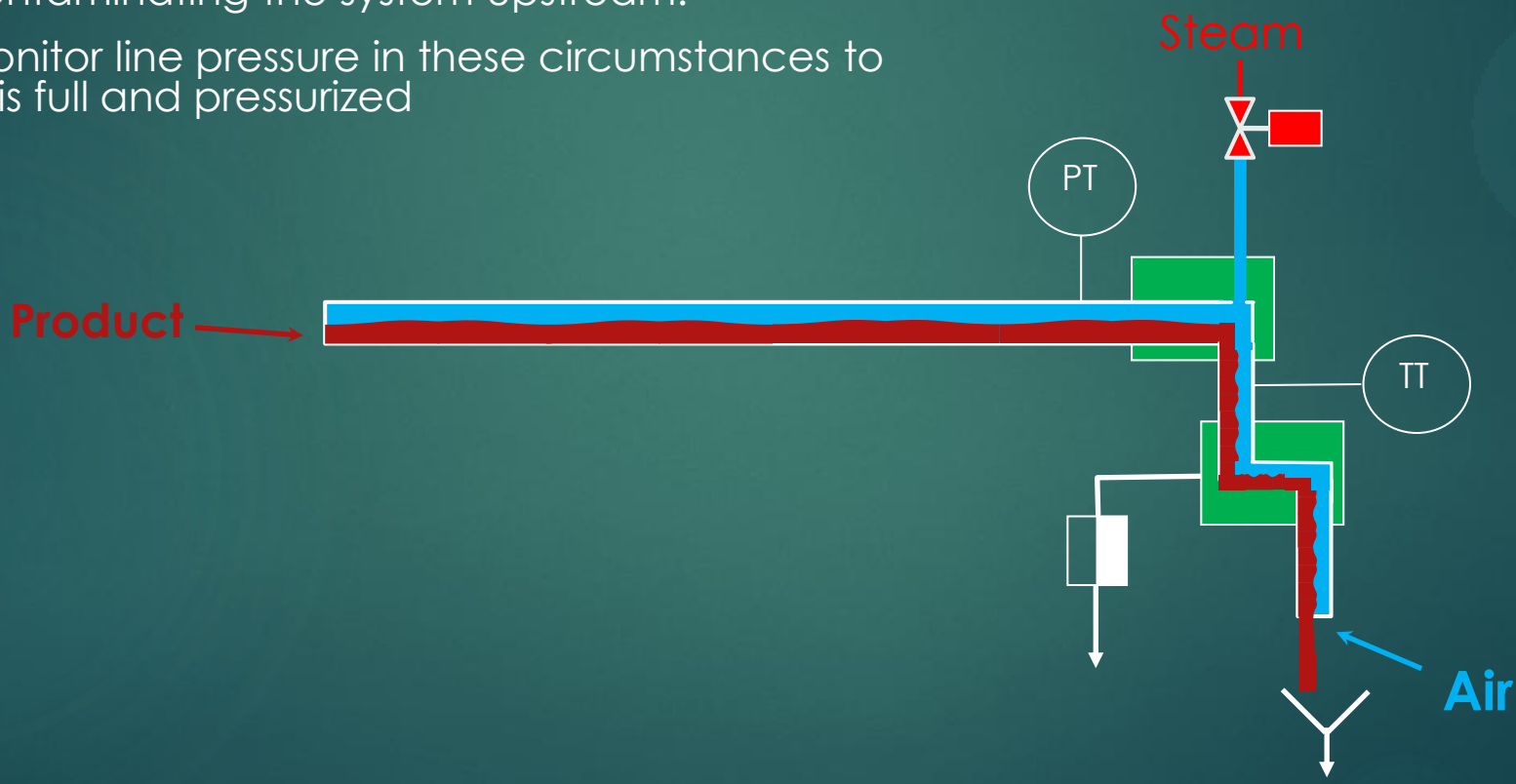
Transitional Phases

- Transitions in an aseptic system can lead to potential for contamination
- Examples –
  - Aseptic tank cool down after sterilization
    - Collapsing steam could create vacuum conditions
  - Production Startup and Product-to-Water Transitions
    - Valve transitions can open unwanted pathways
  - Product changeovers
    - Line flushes to drain should ensure the line is full and pressurized



End-of-Line Flush to Drain

- Insufficient flow to keep the line full and pressurized when going to drain can lead to environmental air bleeding back into and contaminating the system upstream.
- Need to monitor line pressure in these circumstances to ensure line is full and pressurized



Where to Apply Sterile Barriers

- Stationary seals
- Seals on rotating shafts and other moving parts
- Valve seats

Stationary Seals

- Sterile barriers should be put on stationary seals where a risk assessment determines that there is a likelihood of the seal failure
- Sterile barriers on stationary seals were used more in the past particularly on things like aseptic pump face seals and aseptic surge tank door seals
- Risk assessment and experience over the years have shown that sterile barriers on stationary seals are not normally required particularly in systems where the aseptic zone is maintained under higher pressure than the non-sterile zone
  - However, if there is a leak, just because the flow is from the sterile side to the non-sterile side, it does not mean that a breach of the sterile zone cannot occur
  - Run rules should be developed to deal with leaks in the stationary seals
- Sterile barriers on stationary seals sometimes can be used in equipment such as flash coolers where the aseptic zone is at a lower pressure than the surrounding non-sterile environment

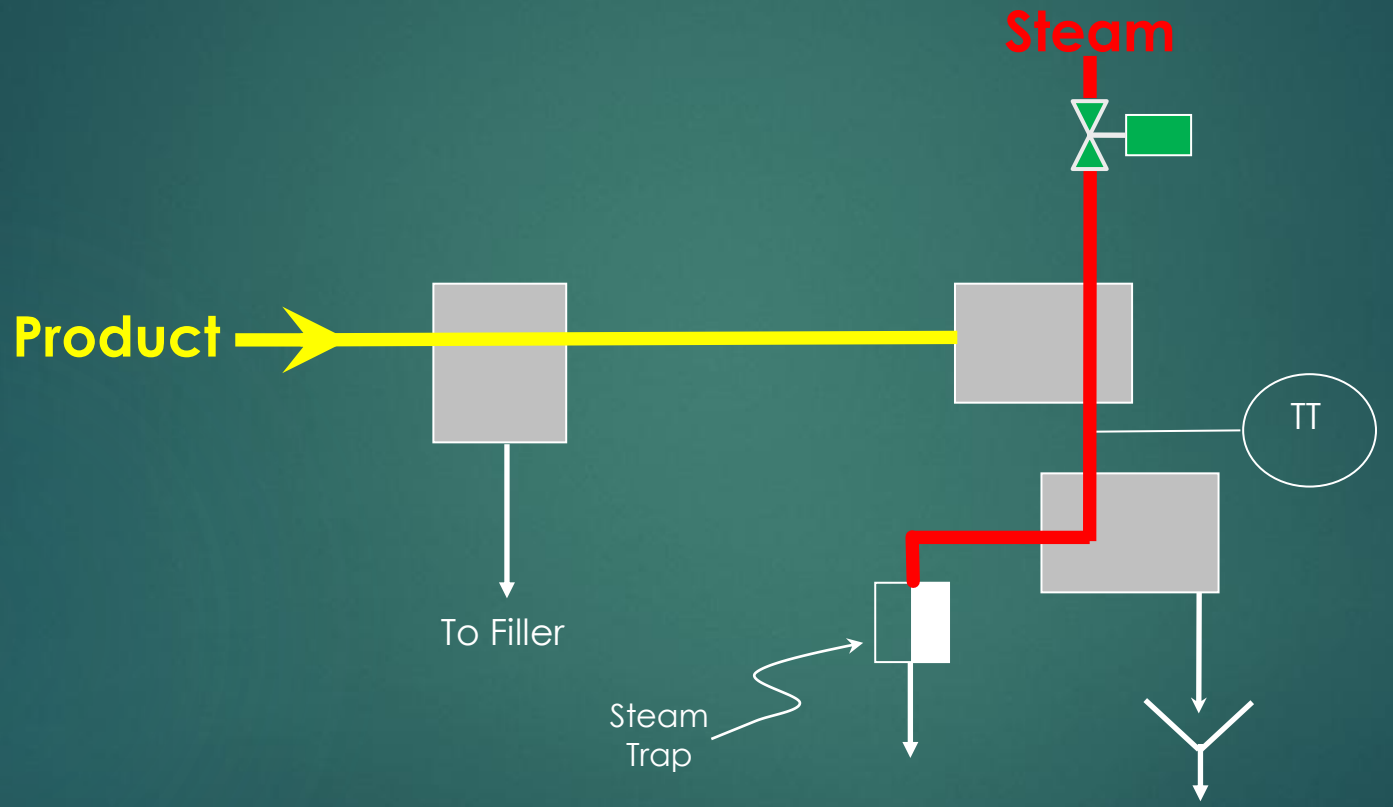
Sterile Barrier Types

- Active steam
- Static sterile condensate
- Static sterile condensate with flush
- Active sterile condensate
- Double valve seal
- Single valve with extended dead leg

Active Steam Sterile Barrier

- Put live (usually low pressure, 15 psig [1 bar]) steam on the back side of a seal with the potential to leak
- Can be monitored by observing steam/condensate coming out of trap, but more commonly with a temperature probe.
- Will often also be monitored as a cold spot during system sterilization
- Examples:
  - Valves where one side of the seal is in the aseptic zone and the other side is not
  - Rotary seals such as on aseptic tank agitators and pump shafts

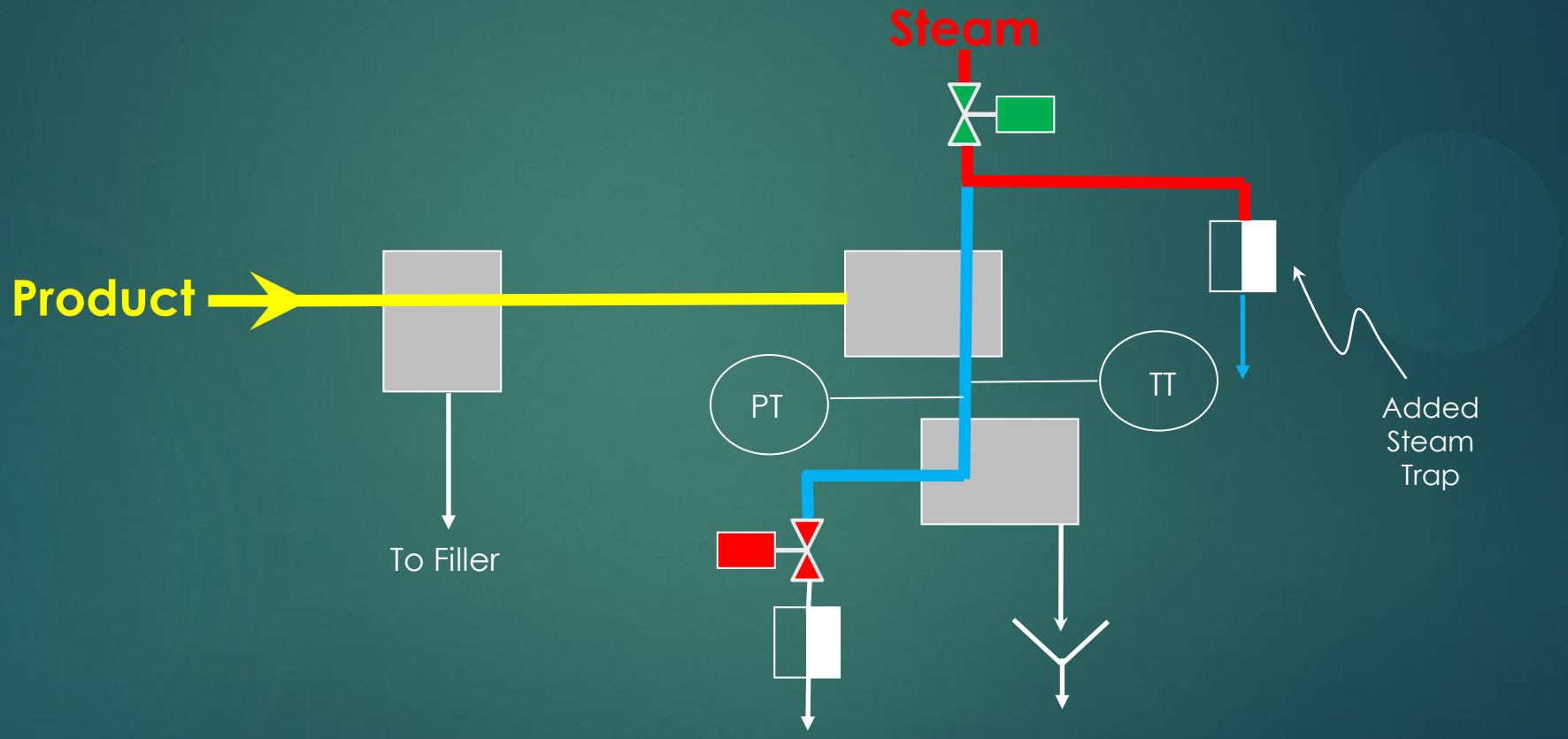
End-of-Line Steam Barrier



Static Sterile Condensate or Cold Condensate

- Similar to active steam barrier but with the steam trap blocked allowing condensate to build up and kept under pressure by the steam supply
- Monitor pressure to ensure it is working
- Useful in situations where excessive heat can cause an issue
- Example –
  - End-of-line barrier where product may sit for an extended period and become burned on and difficult to clean

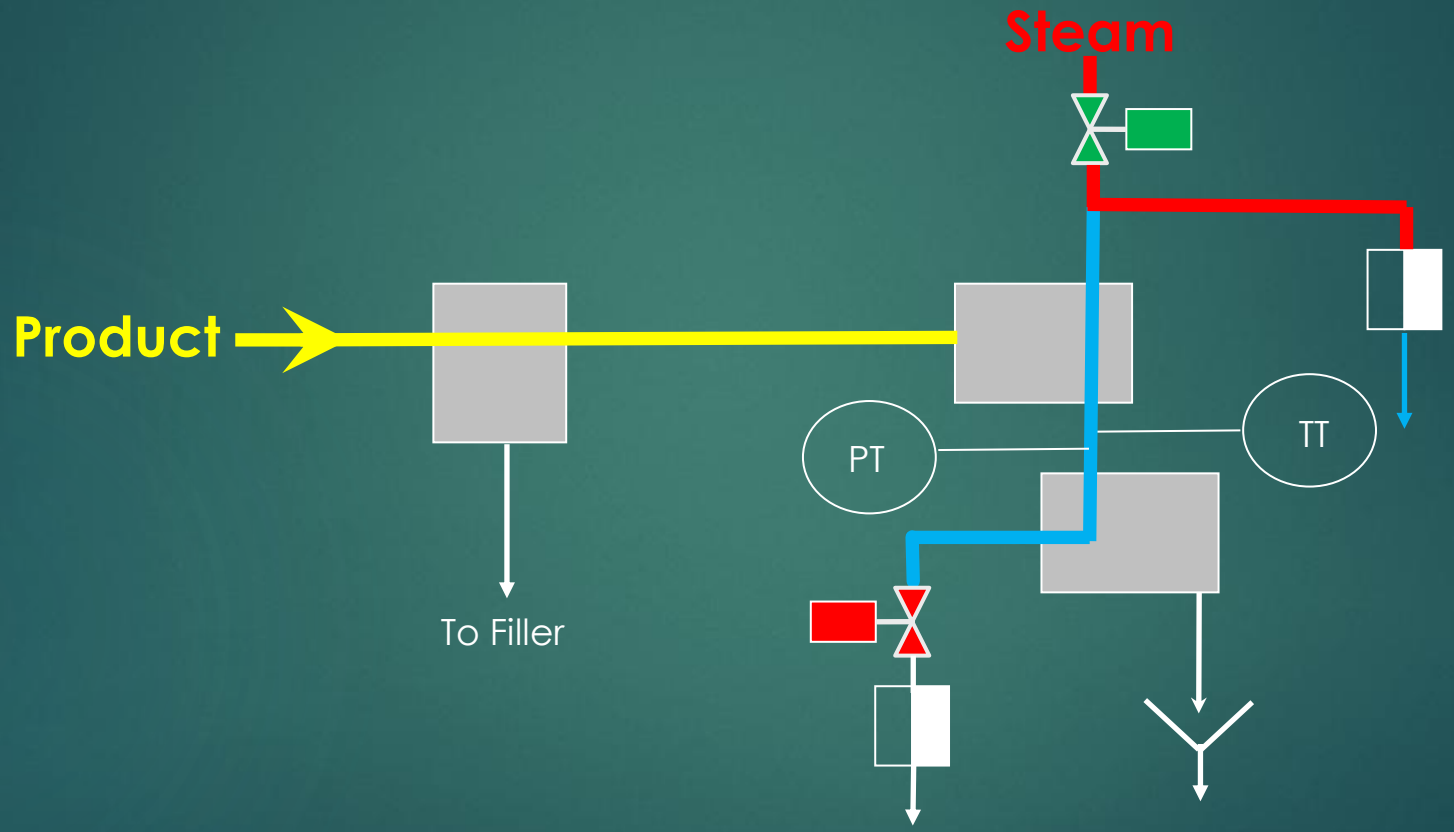
Cold Condensate Barrier



Condensate Barrier with Steam Flush

- A condensate barrier where the valve to the steam trap is periodically opened to allow fresh steam into the barrier before the valve to the trap is closed again
- May need to stop monitoring pressure when valve to trap is open
- Can be programmed to assure temperature is above some minimum (e.g., 160F, 71C) while overall still cooler than an active steam barrier

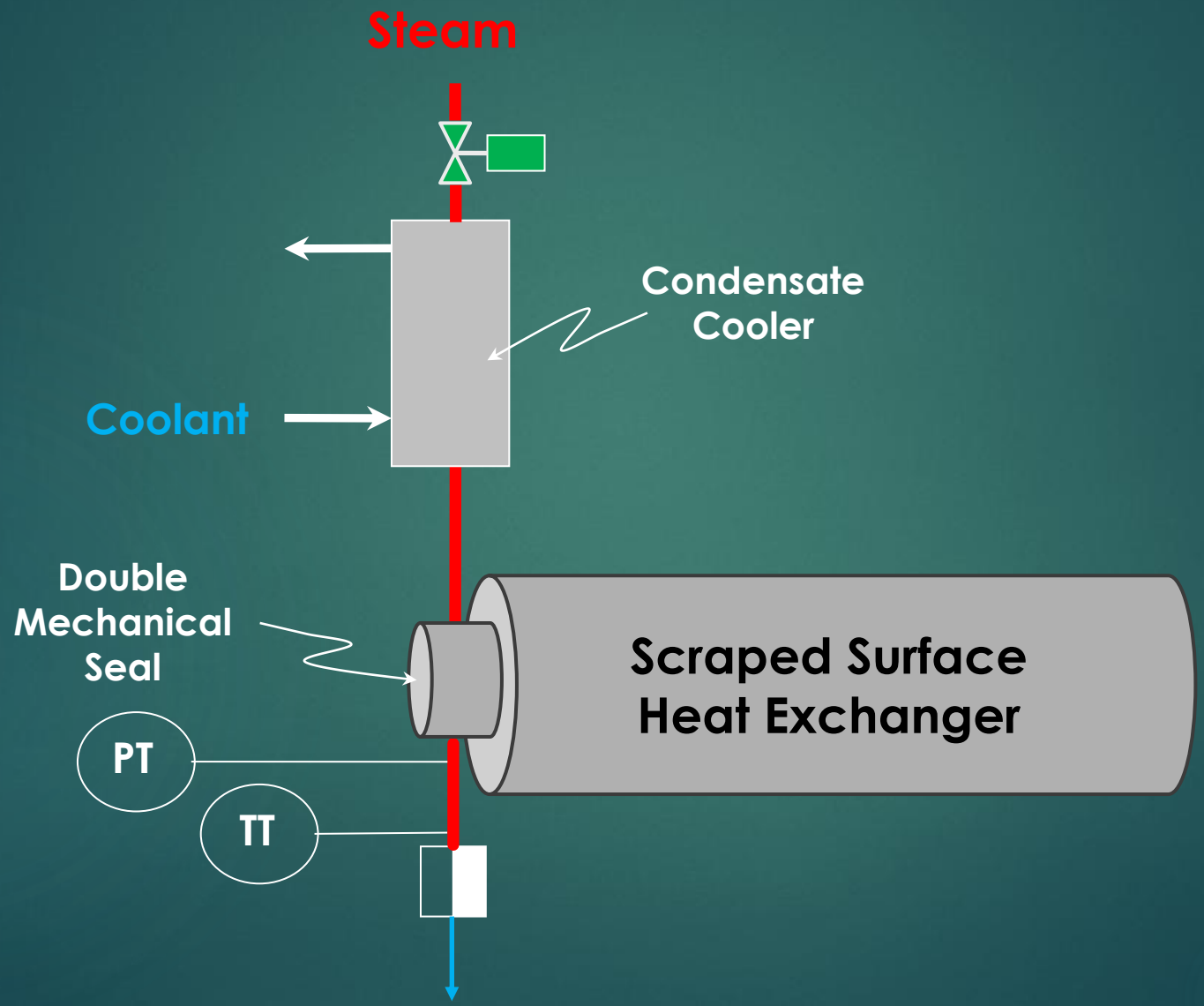
Condensate Barrier with Steam Flush



Active Sterile Condensate Barrier

- A barrier where condensate is created and it constantly flows by the area of concern.
- Condensate is pushed out by supply steam and is kept under slight positive pressure.
- Examples:
  - Rotary seals where exposure to high temperature increases parts wear
  - Valve seals where elevated temperatures are not desired

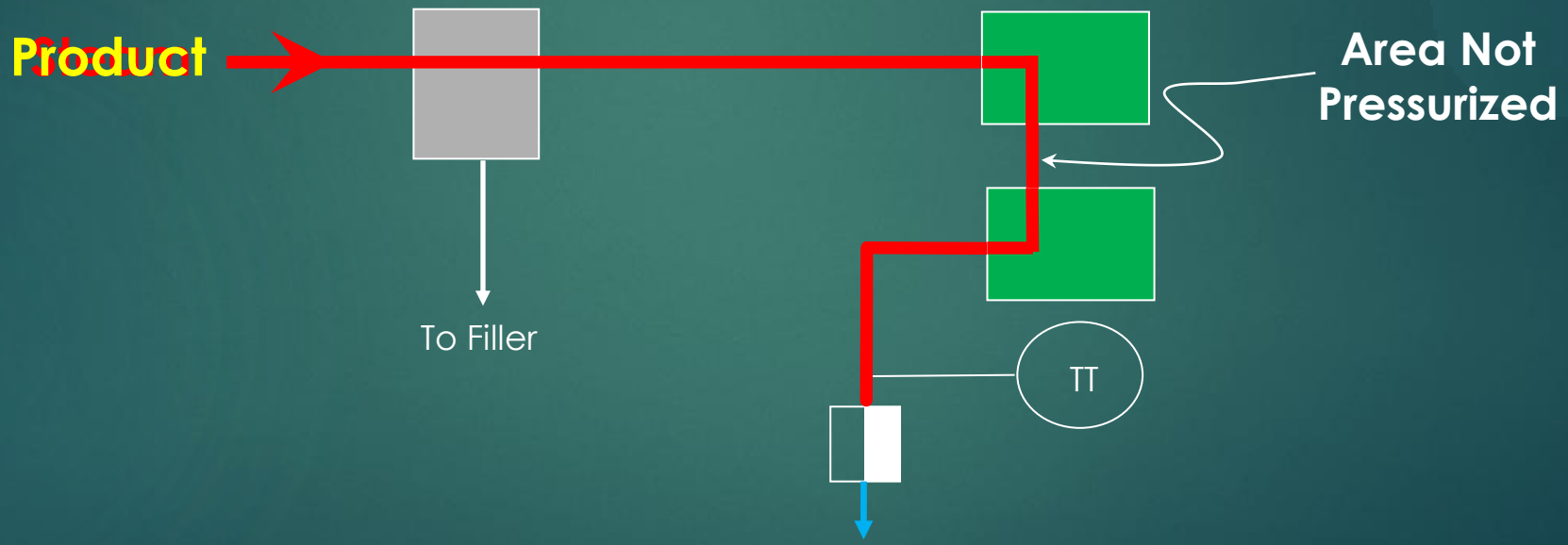
Active Sterile Condensate Barrier



Double Valve Seal

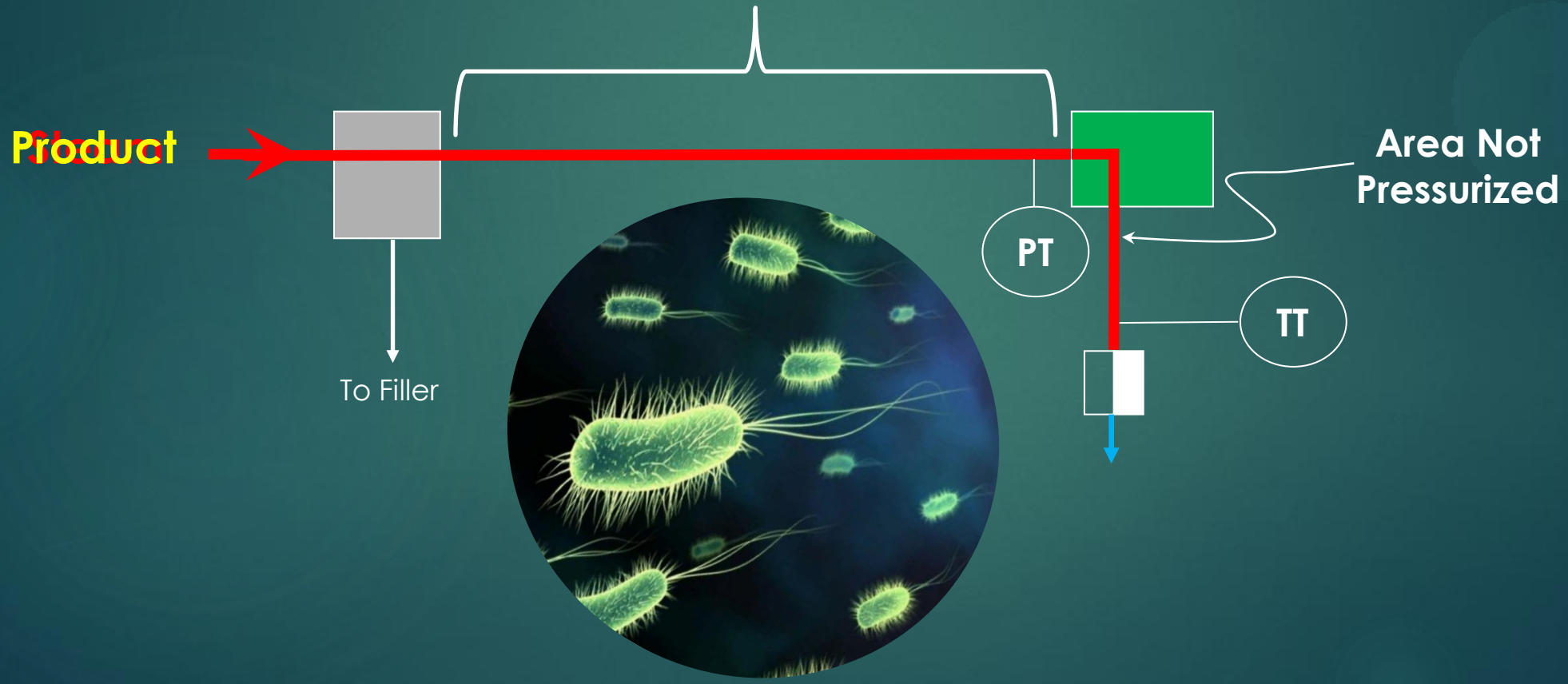
- Concept is to have 2 seals in series where the first seal would have to fail, become contaminated and contamination work its way to second seal and second seal also fails
- Not a common design
- Disadvantages:
  - No direct measure of barrier such as temperature or pressure
  - Line between seals is usually not pressurized and therefore does not satisfy dP design criteria
  - Cannot activate first seal valve during sterile operation as this will contaminate the first seal

Double Valve Seal



Single valve with extended dead leg

Distance too great for microbes to migrate to next point of aseptic product use as determined by the microbial motility rate and the maximum run length



Sterile Barrier Operation

- Barriers can be operated differently under different circumstances
- Example:
  - If a manifold barrier has a product source on either side, the type of barrier could depend on what is happening on each side

Product A Side	Product B Side	Barrier Type
Product	Idle and Empty	Cold Condensate
Product	CIP	Active Steam
Product	Sterilizing	Active Steam
Product	Sterile/Waiting for Product	Cold Condensate
Product	Product	Cold Condensate

Differential Pressure

- Keep product in the sterile zone at a higher pressure than the surrounding non-sterile zone
- If there is a leak, it will be from the sterile zone to the non-sterile zone.
- Pressure can vary from very low (tens of Pascals) to relatively high (a couple of Bars)
- The dP limit is dependent on the situation and the accuracy of the instrumentation
- Examples:
  - In a product to product regenerator, the instrumentation is generally accurate to a few tenths of a psid (a few tens of a millibar) and therefore a limit of about 2 psid (~140 mbar) is appropriate
  - In an aseptic filling tunnel the pressure is much lower and therefore the instrumentation needs to be a lot more precise and measure down to the tens of Pascals and therefore the limits can be in the tens or hundreds of Pascals

Maintenance of dP

- Make sure lines are full and positive dP maintained for transitions (e.g., sterilization cool down, production start up, product change overs, production shut down).
- Make sure there is proper instrumentation
- When measuring pressure at the bottom of a tank, take into account the head pressure of the product in the tank.

Avoid Risky Behaviors

- Avoid complex designs
  - Design for what you are going to do, not what you might do
  - Flexibility often equates to added complexity
    - Consider manual connections (flow panels) versus automated ones (valve clusters)
- Run at steady-state
    - Process supply matched to filler output with appropriate surge
- Have good maintenance and change control programs
    - Timely scheduled maintenance
    - APPROVED replacement parts (don't let procurement dictate)
- Operator diligence
    - Have operators 'walk the lines' and record observations
    - Operators trained on critical factors, potential faults and appropriate reactions

Sterile Barrier Failure

- What is the proper reaction?
  - Automatic immediate shut down
  - Operator initiated shut down and/or deviation report
  - Delay time to allow for re-establishing the barrier
- Run rule guidelines for different situations and barrier designs would be helpful
  - What are the risks of product contamination for different leak types and scenarios?
  - Examples:
    - Leak in a static seal
    - Leak in a static seal that re-sealed itself
    - Leak in a rotary seal
    - Loss of temperature/pressure in a steam/condensate barrier

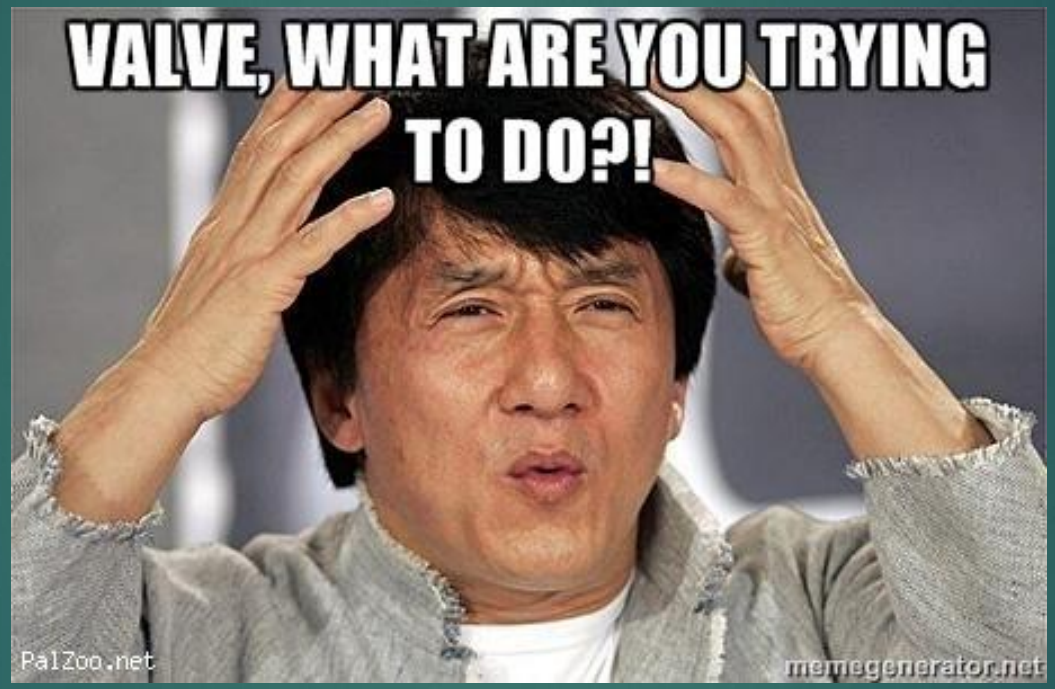
Sterile Barrier Guidance

- Provide design examples
- Suggest operational parameters
- Propose deviation reaction schemes

Conclusions

- There is a lot of institutional knowledge of how to maintain sterility but not as formally documented as achieving sterility
- Success in the maintenance of sterility begins in the design phase of the system
  - Keep the design simple (i.e., keep the number of components in the aseptic zone as low as possible)
  - Design the appropriate sterility maintenance functions (e.g., sterile barriers, dP) and the automatic and/or manual reactions to deviations
  - Consider transitions and how sterility maintenance parameters are maintained and monitored
- Provide operator training and require appropriate diligence
- Guidance on the design, operation and run rules for sterile barriers would be helpful for the industry.

Questions?


VALVE, WHAT ARE YOU TRYING TO DO?!
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