Load type and process/autoclave selection

PDA Europe

Basics and Recent Developments for Autoclaves and Lyophilizers - Tel Aviv/Israel, 13 November 2017

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What load can we treat with an autoclave?

Solid loads

Glassware

Metallic items

- Surgical instruments
- machine parts

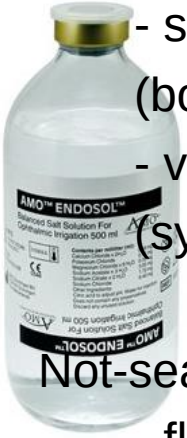
Porous loads

- filters
- textiles
- stoppers in bags (or not),

Liquid loads

Sealed containers (LVP, SVP)

- standard closed containers (bottles, ampoules, vials)
- variable volume containers (syringes)



Not-sealed containers

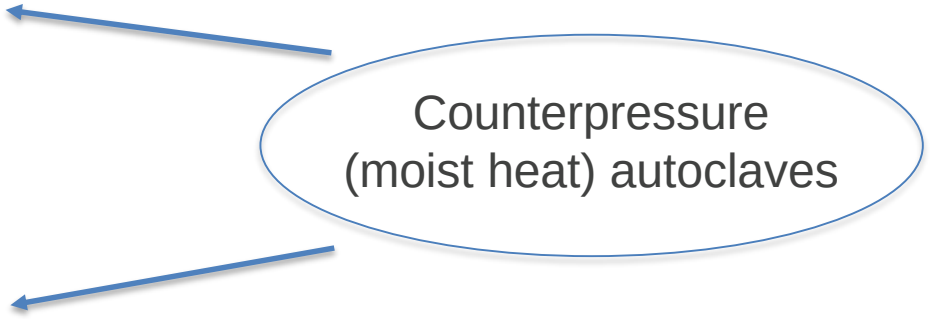
- flask with culture medium
- carboy (with filter on vent)

Moist heat sterilizers/autoclaves

Saturated steam autoclave

Superheated water autoclave

Steam-air mixture autoclave



Moist heat sterilizers/autoclaves

Direct contact

↑

STEAM-MO CONTACT

↓

Indirect contact

Heating & Sterilizing

↑

STEAM FUNCTION

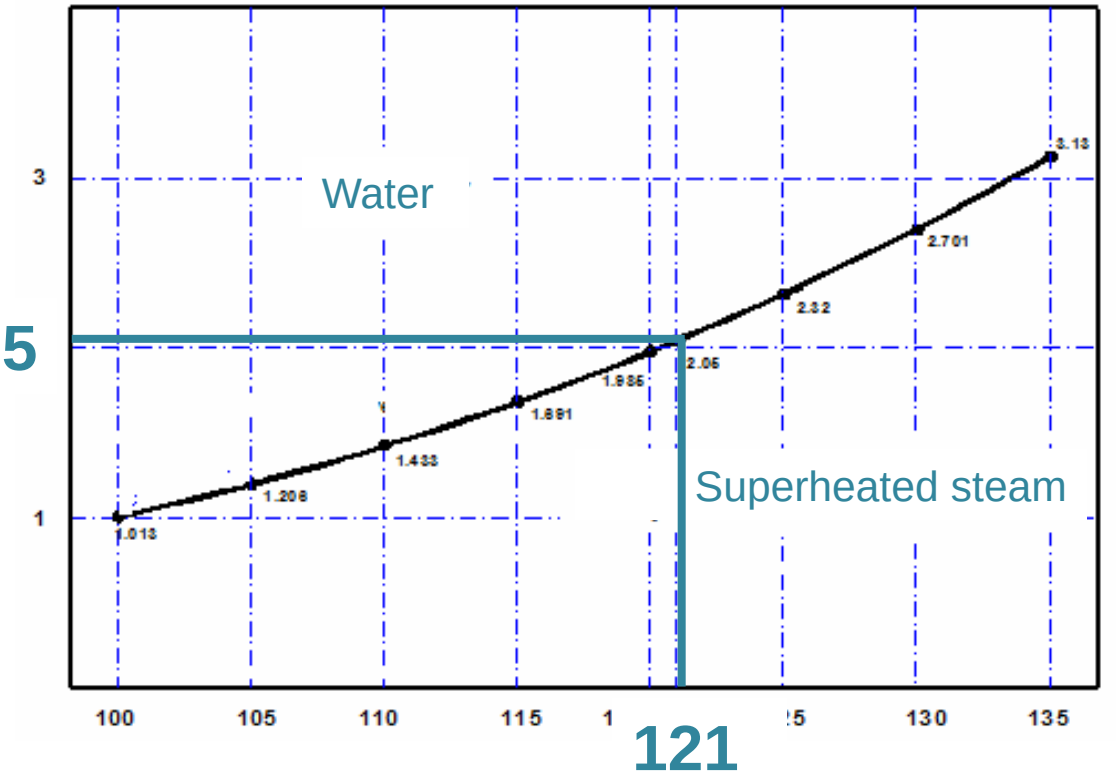
↓

Heating

What is the sterilizing agent?

SATURATED STEAM AUTOCLAVE

The temperature and pressure of saturated steam have a one-to-one correspondence



Saturated steam curve:
water vapour in equilibrium with liquid water at the same T

If you choose the temperature, the pressure inside the chamber is automatically determined!

Temperature and pressure inside the sterilizer chamber

T (° C)	P (bar abs)
110	1.5
121	2.05
135	3.1

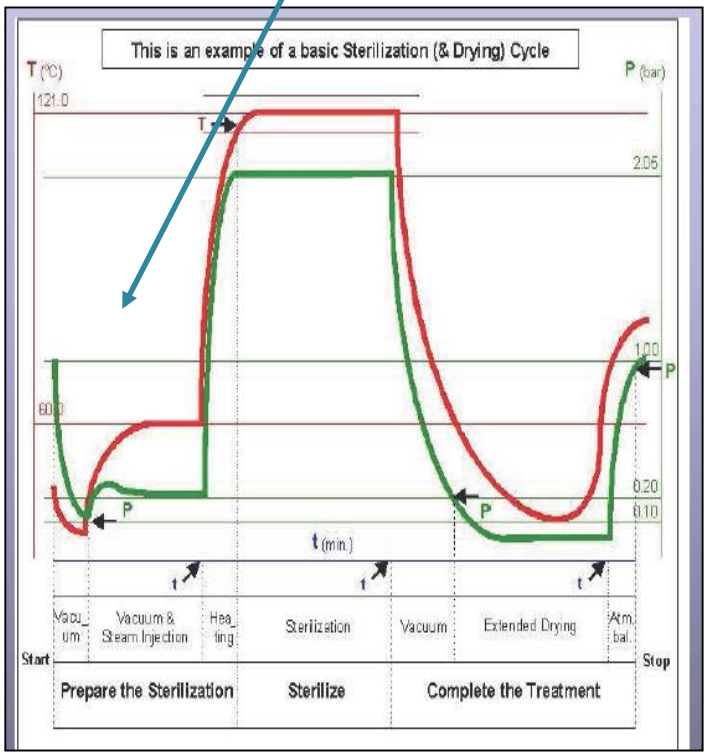
Taking into account steam sterilization requirements…

Steam-MO contact

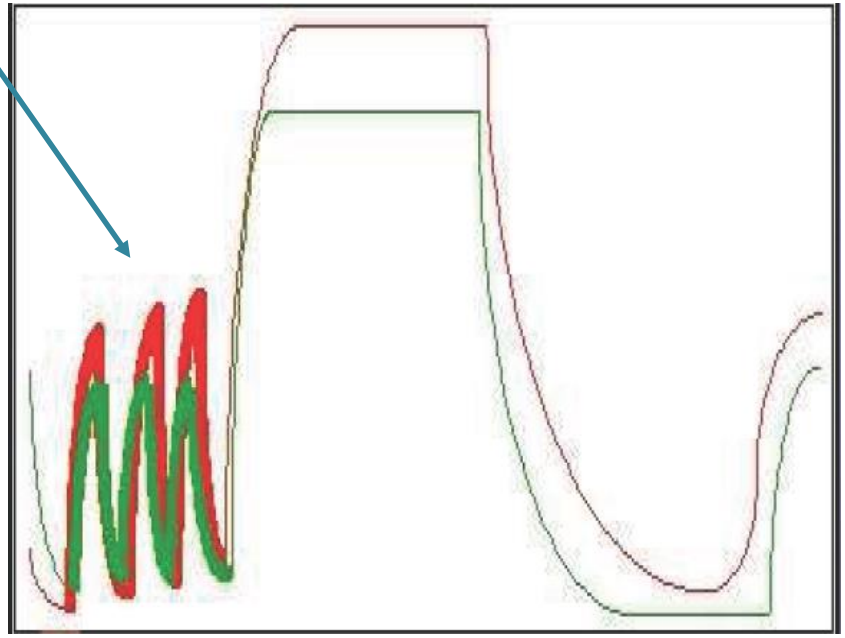
Air must be removed
steam without non-condensable gases

They stratify at the bottom of the chamber because they are more dense than steam; they limit the heat exchange between steam and product

The difference between the two cycles is the method used to remove air (steam injection or steam-vacuum pulses)



Metal items, empty glassware..



Porous solids (where air removal is critical): filters, textiles, stoppers in bag (or not), hollow materials…

Saturated Steam Process: Heating&Sterilization

- ✓ Steam is fed rapidly into the chamber until the sterilization temperature is reached
- ✓ Temperature equilibration/penetration time: delay between temperature of the product (product probes) and temperature of the chamber (monitoring probes)
- ✓ The condensate is continuously removed by a flow of dynamic steam: the vacuum pump always extracts condensate through a small valve
  - ✓ Fresh vapor continuously replaces the removed steam
  - ✓ Excellent stability and uniformity of temperature inside the chamber

The selection depends on the load type and on the final required results (e.g. wet or dry product)

Drying and “natural” cooling by final vacuum (solids or very small sealed containers with liquids, e.g. ampoules)

Indirect cooling by cold water circulation in the jacket and/or in internal heat-exchangers (plates); with air counterpressure (liquids in non-sealed containers)

Direct cooling by water spray onto the load:

- with air counterpressure (liquids in sealed small containers, SVP)
- without air counterpressure (only for liquids in very small sealed containers)

Stoppers in bags

A typical example of a porous solid load to be treated in a saturated steam autoclave

Stoppers in bags

- ✓ Load: *Rubber Stoppers in Tyvek/Plastic bag*
- ✓ Autoclave type: *Saturated Steam Sterilizer*
- ✓ Requirements: *Residual Humidity ≤ 0.1%*

Residual humidity ≤ 0,1 %

- ✓ Strongly needed for freeze dried products
- ✓ no risk of microbial growth
- ✓ to preserve machinability
- ✓ to preserve packaging barrier capability

Humidity in rubber stoppers: potential sources

- ✓ Stopper formulation/matrix
- ✓ Storage conditions (ex. in the sterile area at the filling facility)
- ✓ Sterilization treatment and further processing steps

Stoppers in bags: typical cycle

Before the sterilization phase…

- ✓ Hot air is inserted into the chamber to heat the load and, therefore, to reduce the creation of condense

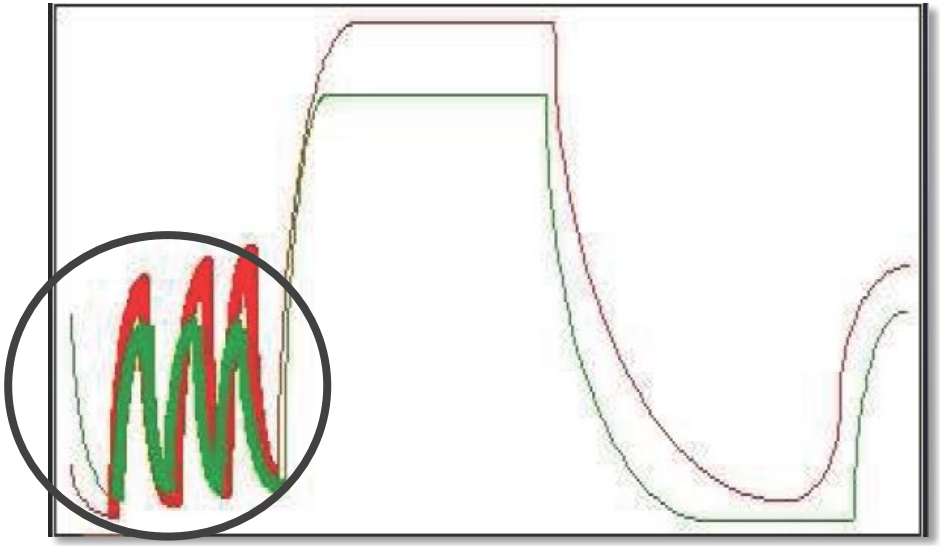
- ✓ The removal of the air is carried-out with a modulated depressurization (to maintain the integrity of the bags) followed by modulated steam-vacuum pulses; the sequence (pulse) is repeated several time

Stoppers in bags: air removal

Air removal by **steam injection**:
Metal items, glassware

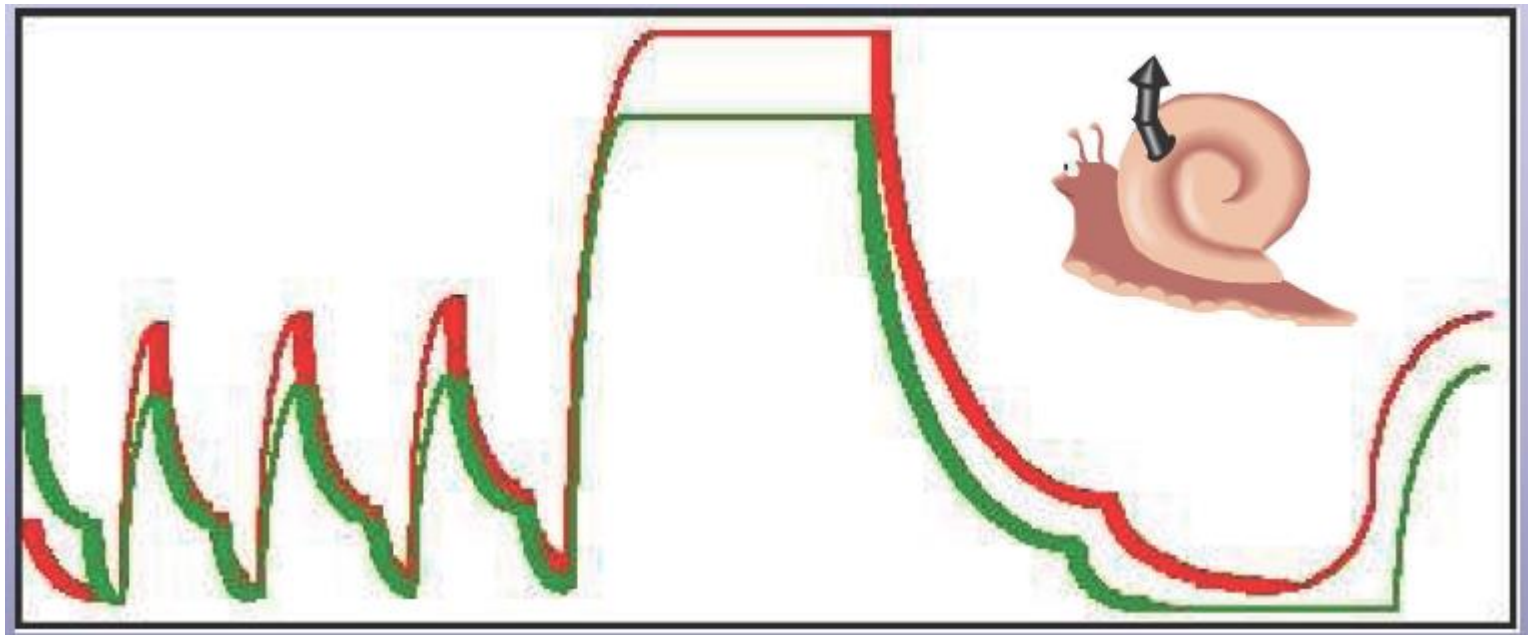
Air removal by **vacuum/steam pulses**: porous solids (where air removal is critical)

STOPPERS IN BAGS

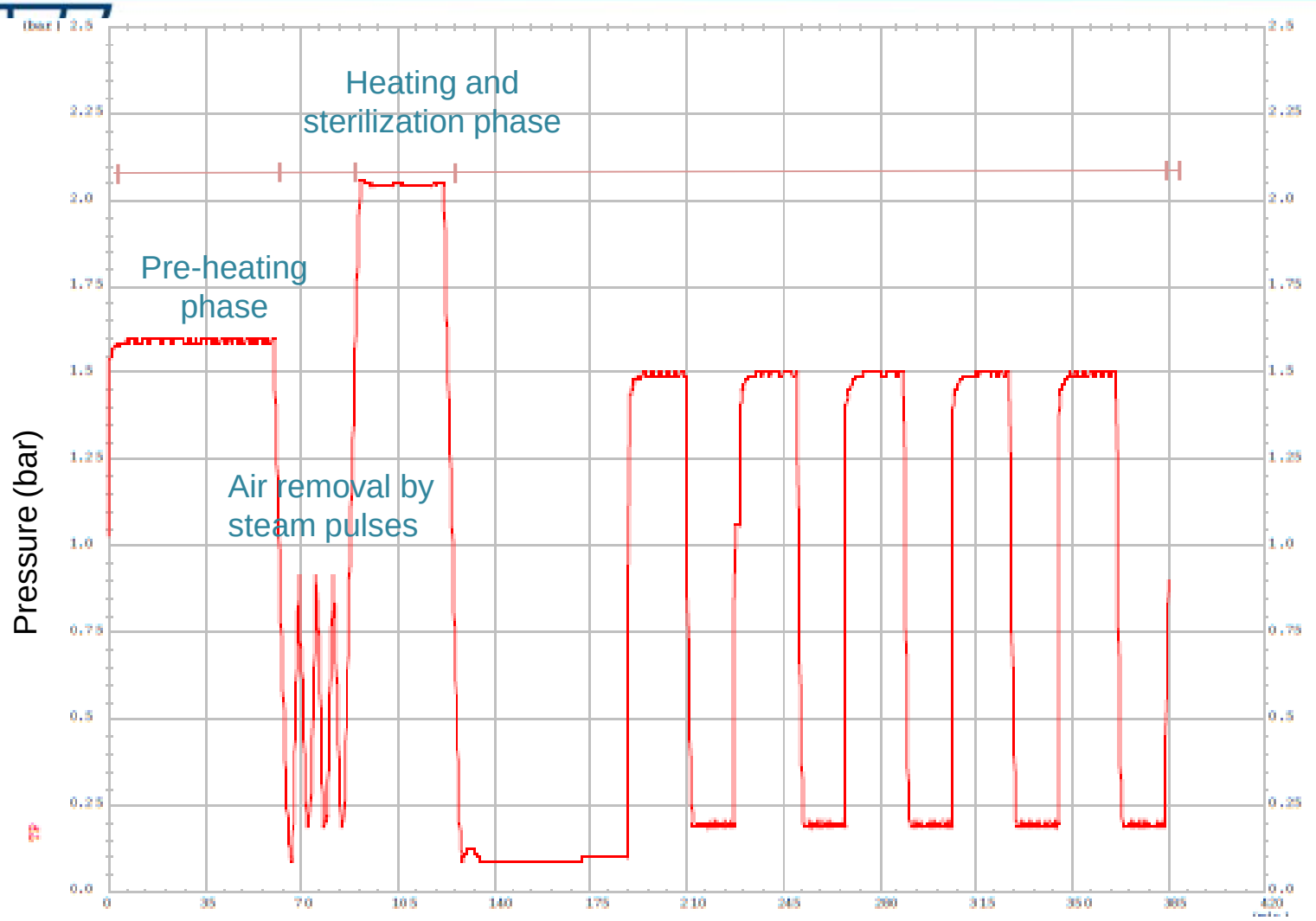


Stoppers in bags: air removal

Cycle with modulated vacuum/steam pulses to not damage the load (e.g. for filters, membranes, stoppers in bags…)



Stoppers in bags: typical cycle



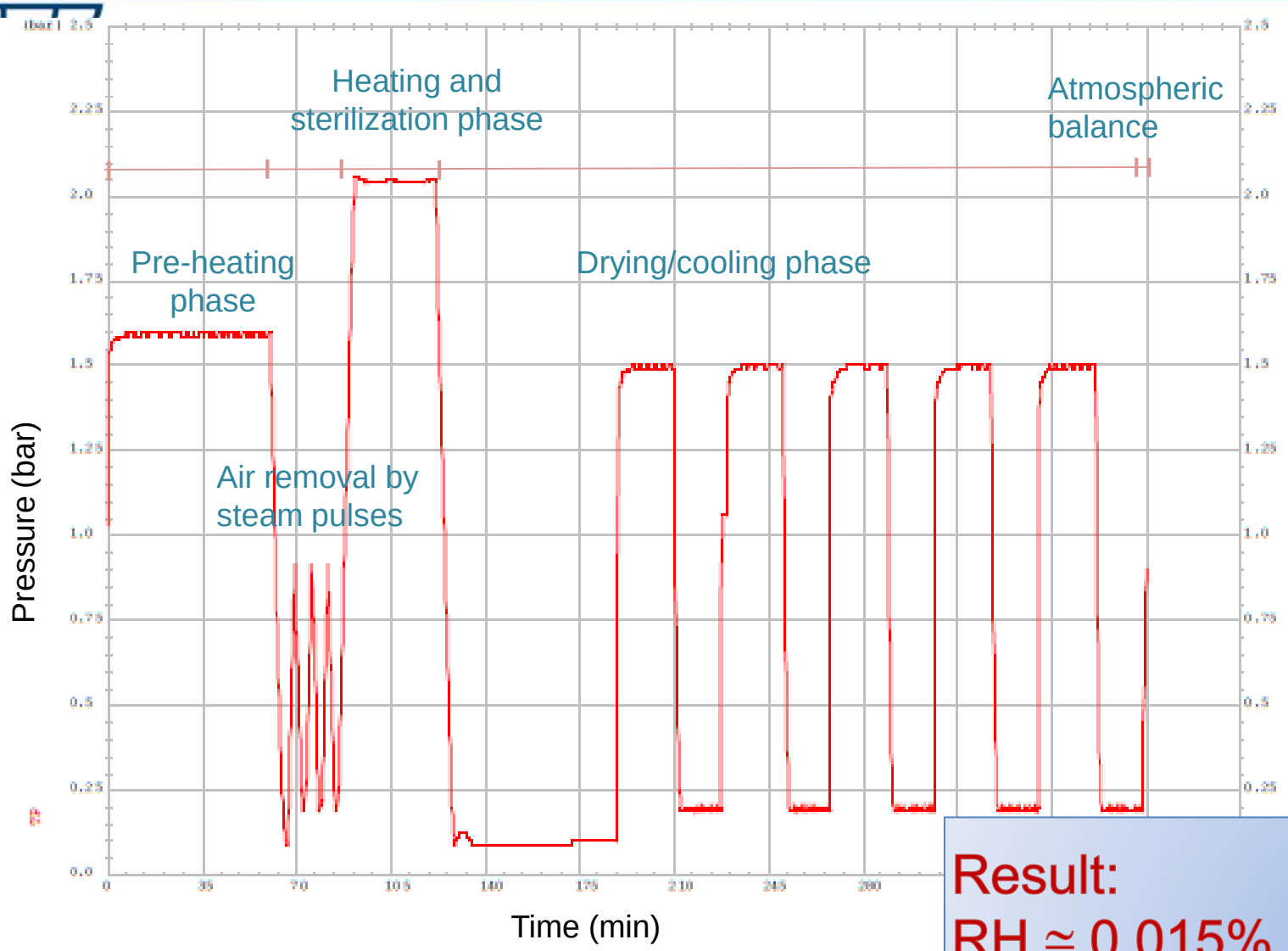
After the sterilization phase…

- ✓ The vacuum causes the rapid evaporation of the condensate deposited on the material; in order to evaporate, this condensate requires vaporization calories which it draws from the material, which therefore cools

- ✓ During these phases the jacket is full of steam, and the heat which is emitted contributes to evaporate the condensate

- ✓ Air is injected into the chamber to help the thermal exchange (the transmission of heat from the jacket is poor because of vacuum)

Stoppers in bags: typical cycle



Result:
RH ≅ 0,015%

Solid load drying: key points

- ✓ Material design & packaging system
- ✓ Item orientation/arrangement
- ✓ Load initial temperature
  (& sterilization temperature)
- ✓ Drying by vacuum improved by:
  - ✓ Auxiliary heating equipment
  - ✓ Vacuum/ (hot) air pulses
  - ✓ Forced circulation of hot air (ex. fan)

✓ Our results after cycle optimization…

Drying phase	Cycle time	Residual Humidity [%]
Jacket (steam) + hot air	298 min	0,228
Jacket (steam) + hot air + FAN	291 min	0,015

+ FAN

A FOF autoclave could be the right choice

Compared to LVP, they are more resistant to pressure differences: the resistance decreases as the diameter increases

What are the other options to perform the cooling ?

Indirect cooling
by cold water circulation in the jacket and/or in plates with air counterpressure

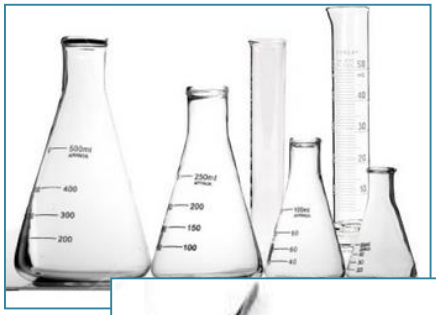
Direct cooling
by water spray with air counterpressure

The choice depends on costumer needs (i.e. cycle time, final unloading temperature, product unloaded wet or dry) !

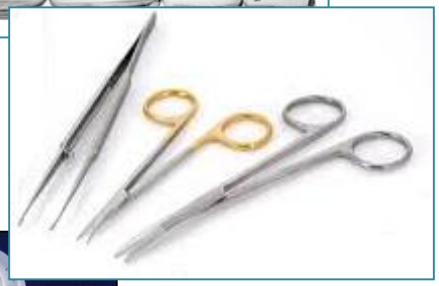
SOLIDS

Hard/Porous loads

- ✓Glassware, plastic tools (empty)



- ✓Metallic items (machine components, surgical instruments, tools)



- ✓Filters

- ✓Textiles

- ✓Stoppers in bag (or not)

- ✓Wrapped items (steam permeable wrapping)

LIQUIDS

- ✓ Culture media

(not sealed containers)

- ✓ Glass ampoules

They resist to the overpressure!

- ✓ Glass vials

COUNTERPRESSURE AUTOCLAVES

PHARMA

INDUSTRIES

FOOD

INDUSTRIES

The total pressure (P) generated inside the sealed container at the temperature T (ex. 121 °C) is equal to:

$$P = Pv_{(T)} + Pa_{(T)}$$

Pressure of the water vapour

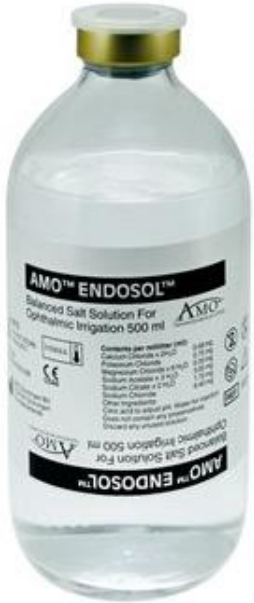
Pressure of the air

1) air initially present in the head space; 2) dissolved gases that come out of the solution; 3) reduction of the head space due to the thermal expansion of the liquid

*Sealed= hermetically closed

Bottle partially filled with water solution at 20°C and 1 bar abs subjected to a saturated steam sterilization at 121°C

Total pressure in the chamber:
Partial steam pressure= 2,05 bar



Partial steam pressure = 2,05 bar
Partial air pressure= 1,34 bar

Total pressure in the bottle ≅ 3,4 bar

$\Delta P \cong 1{,}4$ bar $\rightarrow 1{,}4$ kg/cm^2

The total pressure inside the chamber is automatically controlled and adjusted according to:

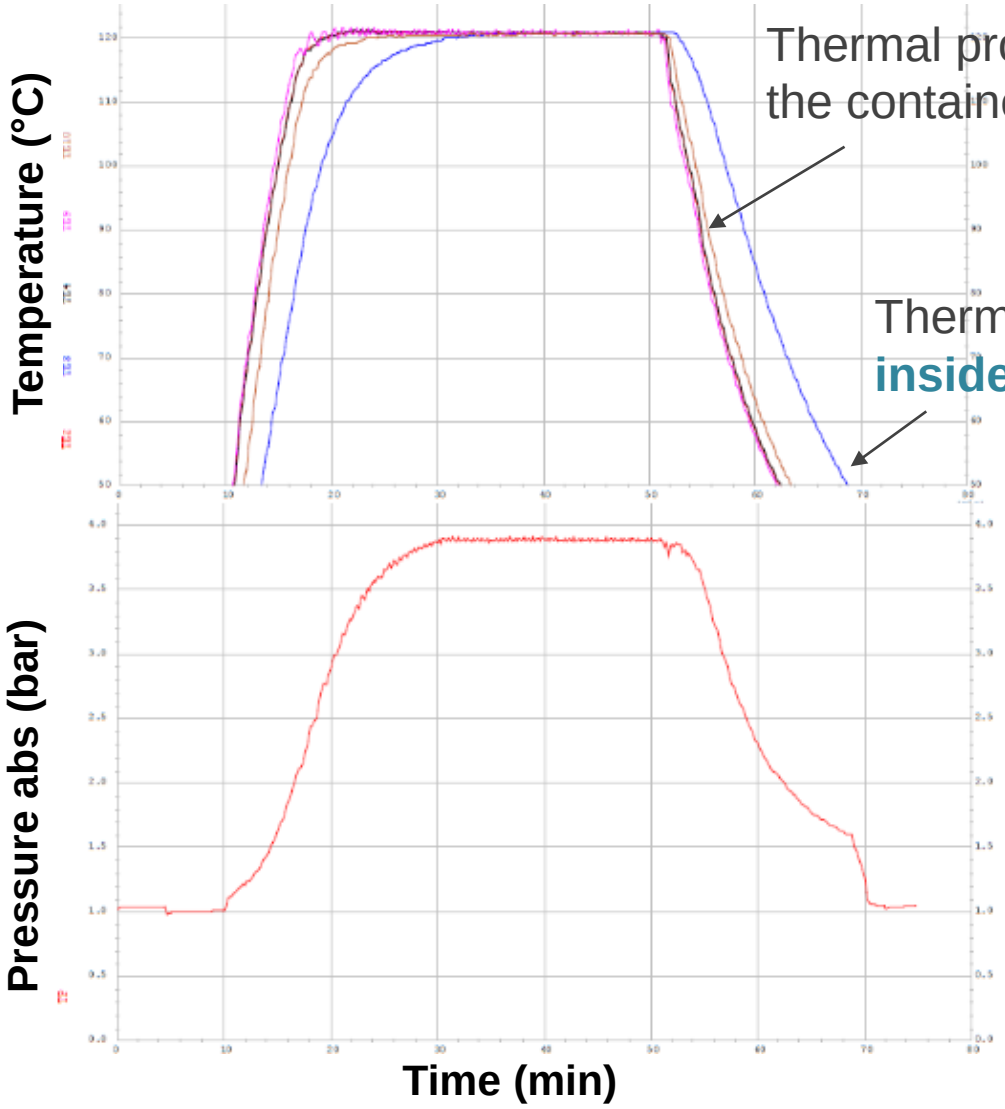
- ✓ **Temperature of the solution**
- ✓ **Container features** (ex. rigid or deformable material)

✓ Steam-air mixture autoclaves

- Should the load be unloaded dry?
- Should the load temperature transition be fast?

✓ Superheated water autoclaves

Counterpressure Sterilization Cycle

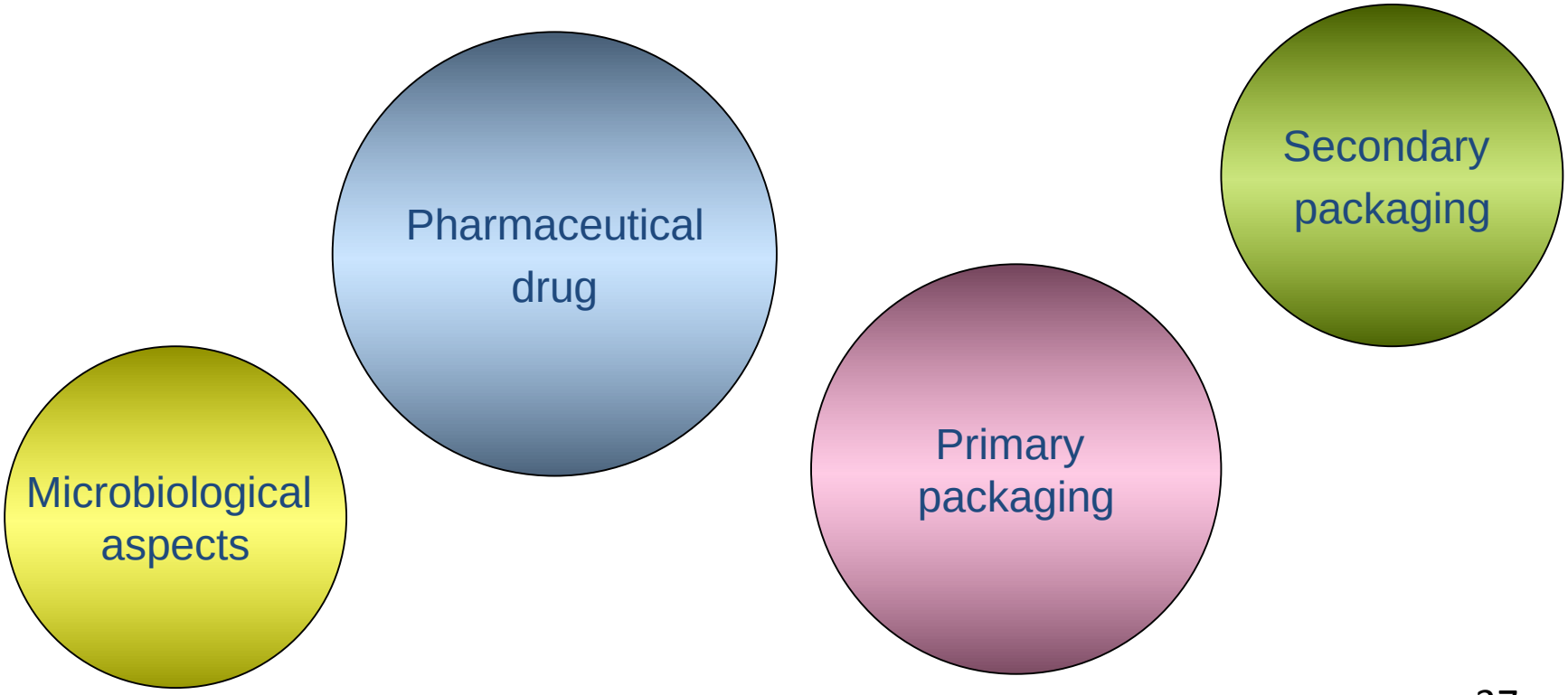


Cooling under pressure is always used but…

- ✓ Superheated water autoclave: DIRECT cooling by water spray
  - Product is unloaded wet
  - The cooling phase is faster (heat exchange occurs through a liquid: more efficient)

- ✓ Steam-Air mixture autoclave: INDIRECT cooling by forced air circulation (fan) + cold water circulation in the plates and jacket (if present)
  - Product can be unloaded dry
  - The cooling phase is longer (heat exchange occurs through a gas: less efficient)

The main issues to consider while sterilizing PFSs with a moist heat process are:



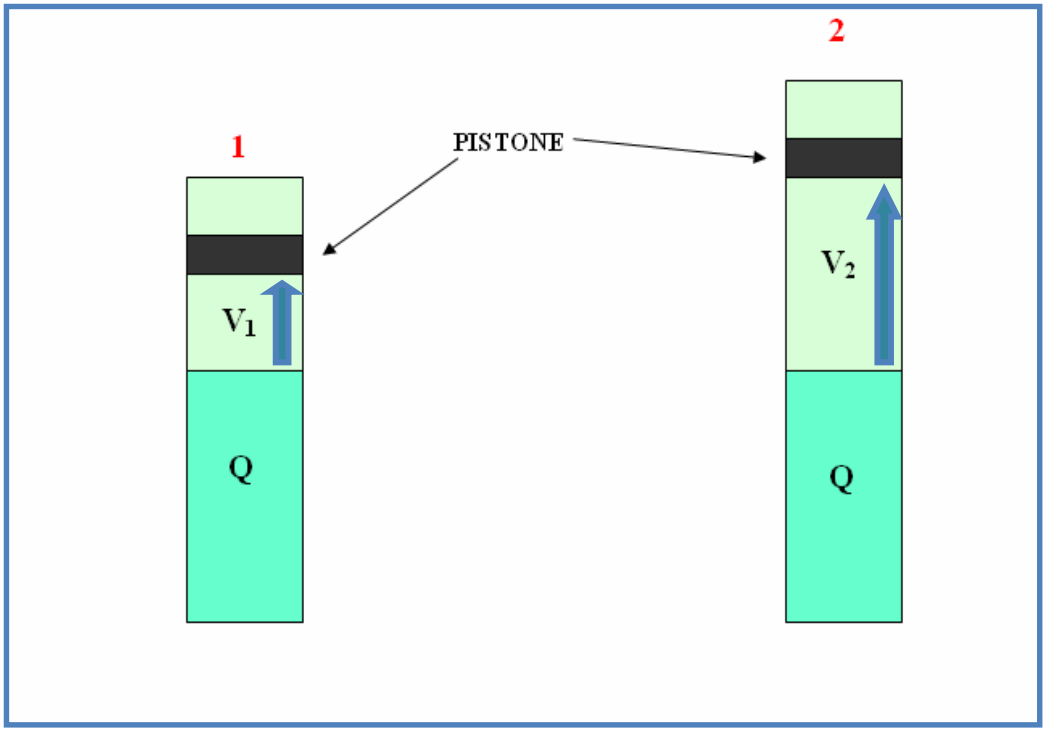
How to avoid

plunger expulsion

during treatment

The head space and the space behind the plunger is small

Container sealed with a plunger: variable volume container



Q= amount of liquid

V_1= head space volume for container 1

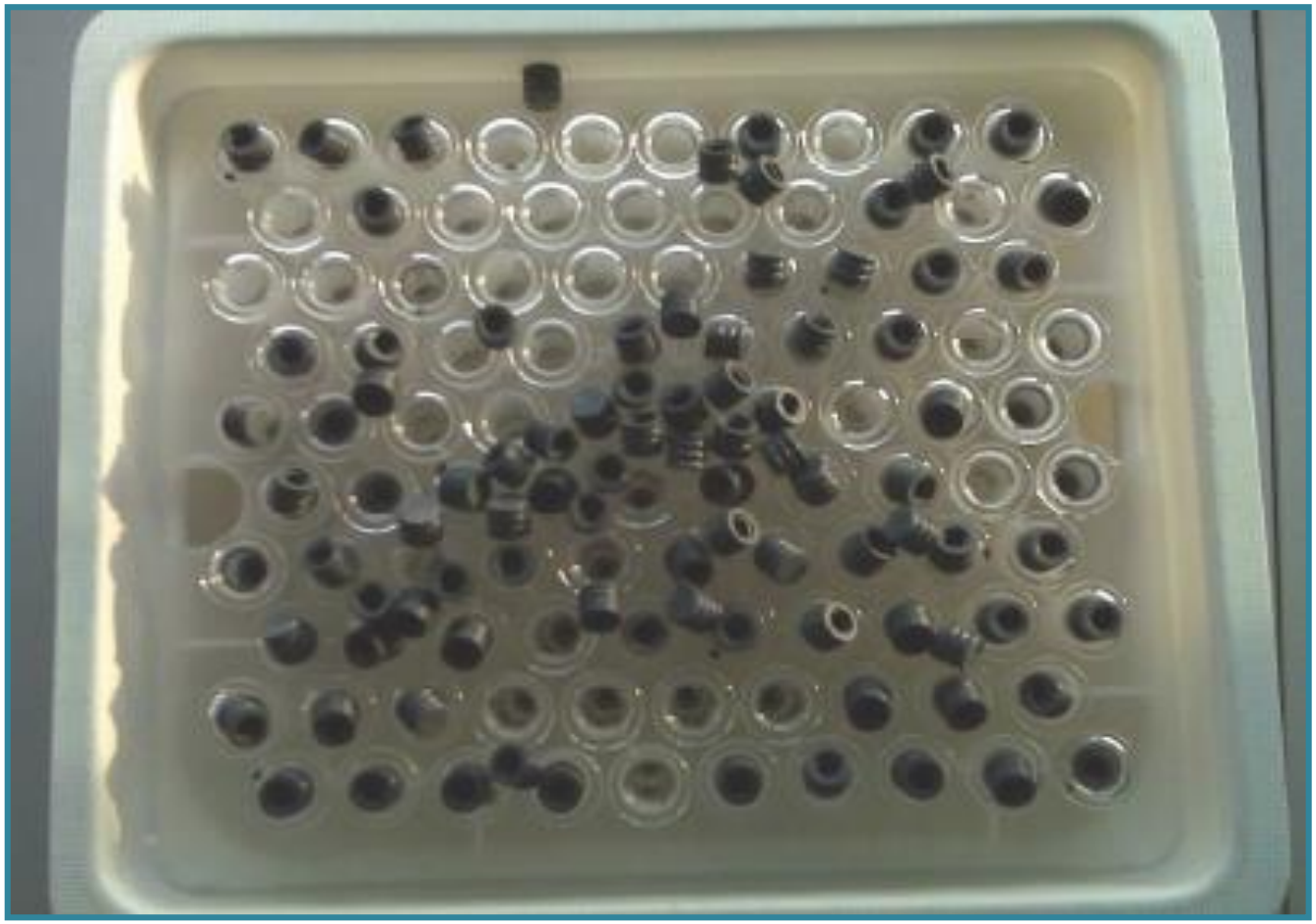
V_2= head space volume for container 2

PRESSURE on PLUNGER 1 > PRESSURE on PLUNGER 2

An aqueous solution increases its volume about 6% when heated from ambient temperature to 121°C
Therefore…

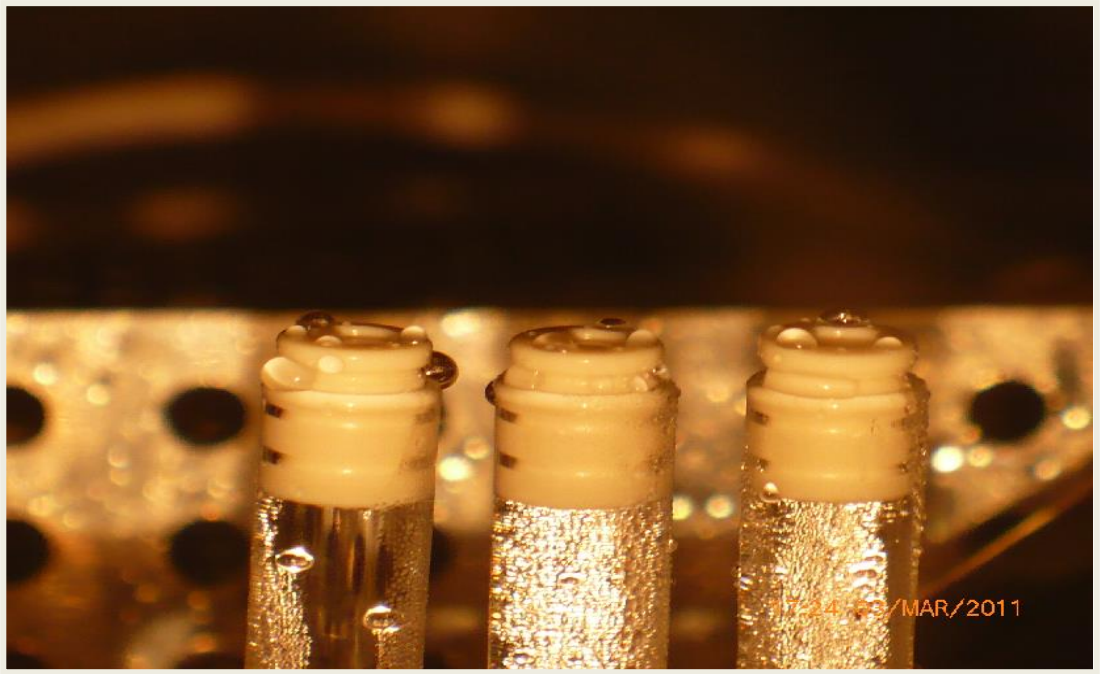
Thermal expansion of the water becomes important if the head space is lower than 10-15% of the volume of the container

Pre-Filled-Syringes



There is no practical mean to prevent the thermal expansion of liquids during sterilization

The pressure required to reduce of 6% the volume of a liquid like water would be very large: thousands of bars !!!



FAQ

- ✓ Is the material resistant to high temperature?
- ✓ What is the melting point of the material?

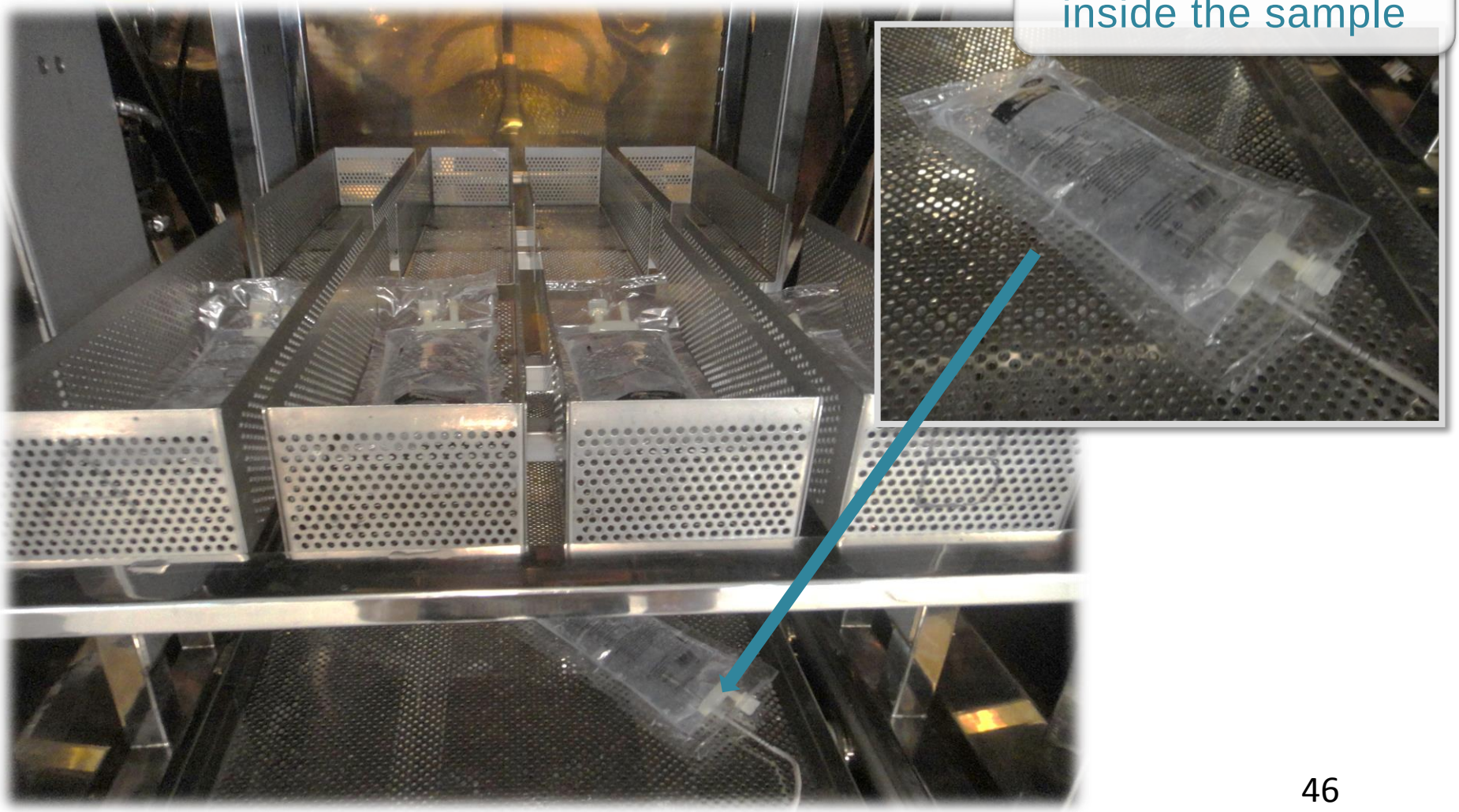
The answers can tell us if steam sterilization is the right choice and how to develop the sterilization process

What happen if…

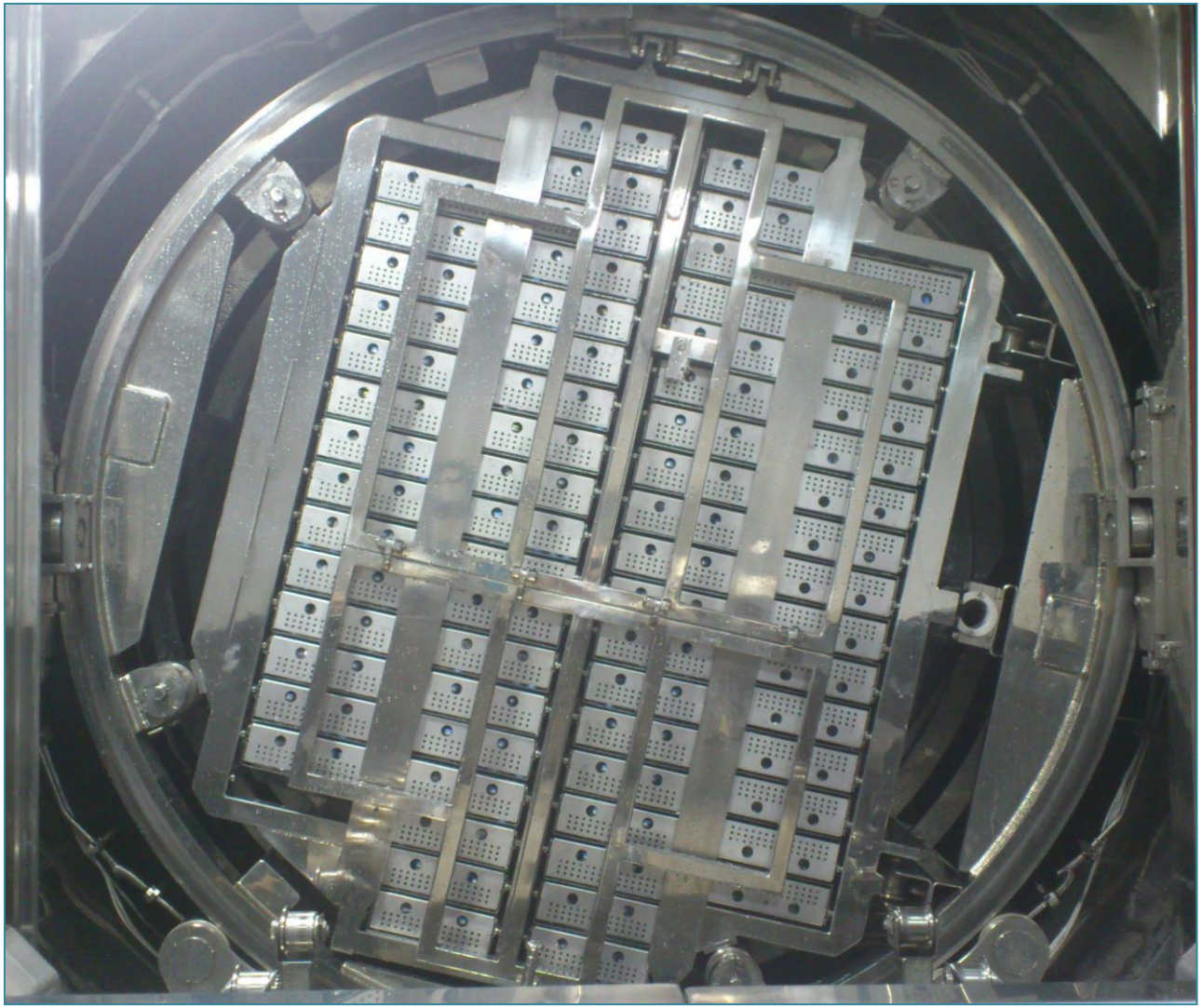
- ✓ Temperature is too high?
- ✓ The applied counterpressure is not well adjusted?

Container deformation

Aqueous solution in double bags



Rotating basket for liquids. Why??



Rotating basket for liquids. Why??

Emulsions, Suspensions

Dense or non homogeneous mixtures

Heat sensitive products (sometimes)

Superheated water autoclaves

- ✓ Easy control of heating and cooling rate
- ✓ Short process duration
- ✓ No consumption of clean steam (used only for filter sterilization)
- • Product is unloaded wet
- • Higher water consumption (for initial filling)
- • Blushing phenomenon (i.e. whitening of the PVC due to water absorption)

Steam-air mixture autoclaves

- • Indirect and 'difficult' control of heating and cooling rate
- • Longer process duration (mainly because of indirect cooling)
- • Consumption of clean steam
- ✓ Product could be easily unloaded dry
- ✓ No PW/UPW/WFI water consumption
- ✓ Blushing phenomenon very rare

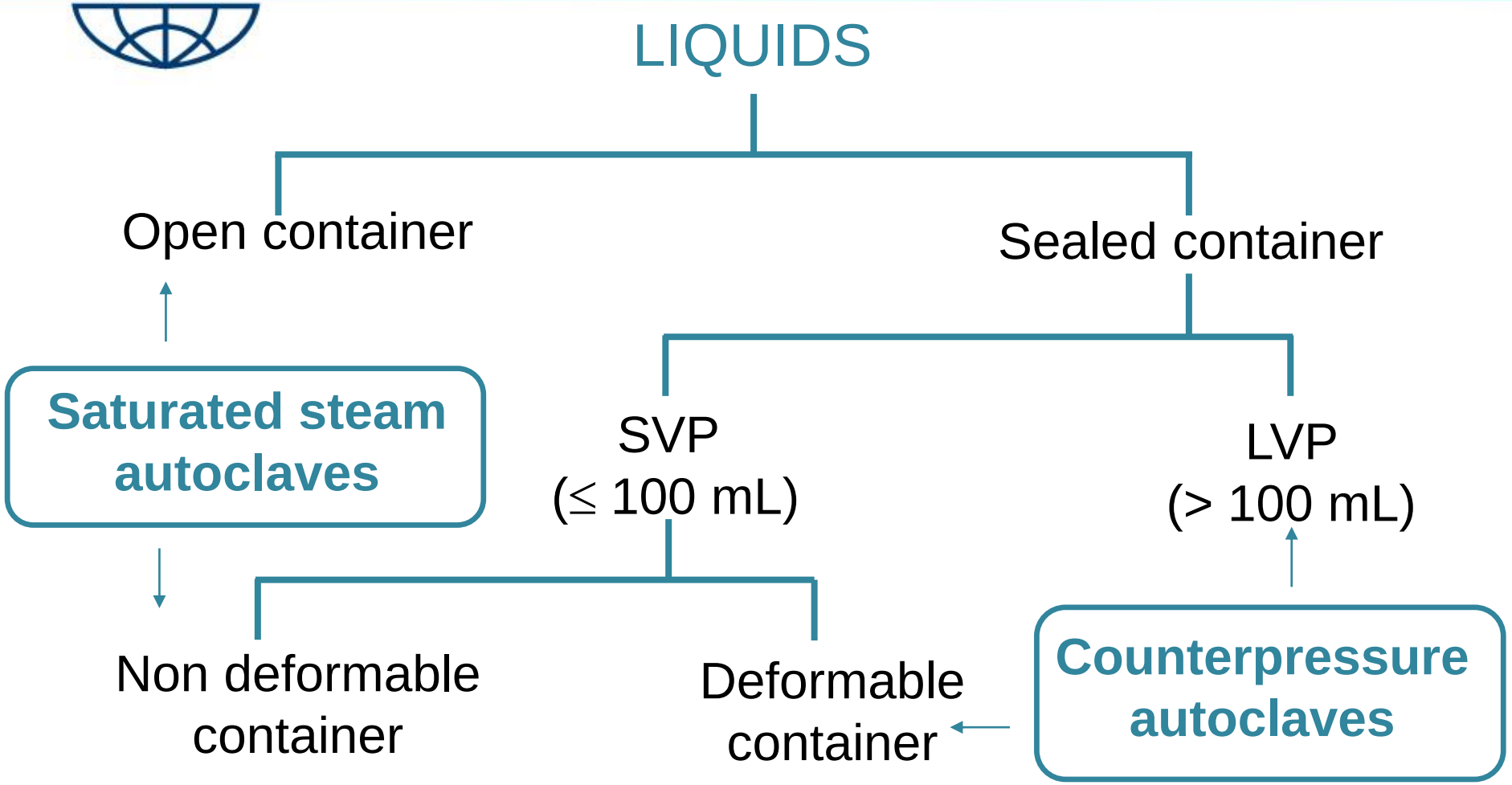
If your load is compatible with moist heat sterilization conditions (ex. temperature, pressure and humidity) you must use this method to sterilize it

Is your load resistant to overpressure?

Yes → Saturated steam autoclaves

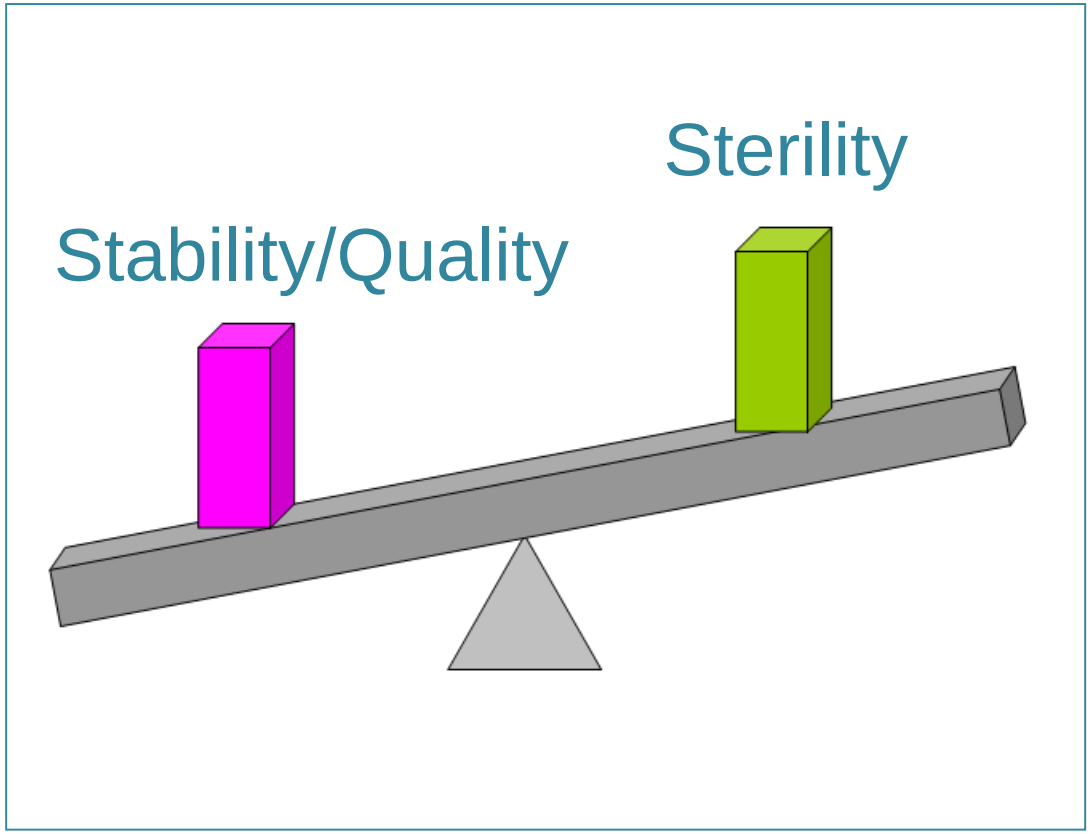
No → Counterpressure steam autoclaves

- ✓ Is the product **solid** or **liquid**?
- ✓ What are the characteristics of the **container**?
  - Plastic or glass material
  - Sealed container (ex. «standard» sealing or variable volume container) or open container
  - Large or small volume
- ✓ Should the product be unloaded **dry** or **wet**?
- ✓ Does the product need to be **rotated**?



SVP= Small Volume Parentals
LVP= Large Volume Parentals

Sterilization is a compromise



Thank you

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