

Theory 1

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2020 PDA EUROPE TRAINING COURSE

Freeze Drying in Practice



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Theory 1

- Why lyophilization?
- History and Development
- Examples in daily life and pharmaceutical industry
- The freeze drying process
- Freeze drying equipment
- Pros and Cons for Lyophilization



Why drying?

- Drying for stabilization of products for long-term storage:
 - Reduced mobility decreases tendency for physical instabilities
 - and decreases chemical degradation, e.g. hydrolysis
- Drying techniques
 - A. Evaporation
(not suitable for sensitive biologics)
 - B. Spray drying
 - C. Vacuum drying
 - D. Freeze drying / lyophilization**
 - Gentle procedure for thermo sensitive molecules to remove water
 - Basic principle: Removal of water after freezing under vacuum by sublimation (and desorption)





Abb. 1: „Ötzi“ (Foto: Archiv Südtiroler Landesmuseum, www.iceman.it)

Mummification by cold and dry air flow

Freeze drying



Chuño = frozen potatoe

- Freeze dried, long-life food from the Andes made from potatoes
- Produced at low water vapor pressure at high altitude
- Origin already during Inca's time

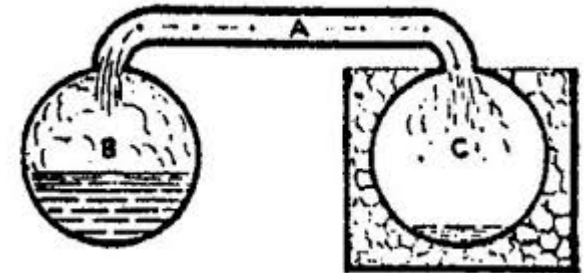
Vacuum freeze drying

PHILOSOPHICAL
TRANSACTIONS:

On a Method of Freezing at a Distance

William Hyde Wollaston

Phil. Trans. R. Soc. Lond. 1813 103, 71-74, published 1 January 1813



William Hyde Wollaston:
Cryophorus



Examples in food industry



→ Preserve color and taste



Aerospace food



→ Instant products



Examples in daily life

Archeology



Documents after water damage

Conservation:

- Preparation of animals
- Decoration





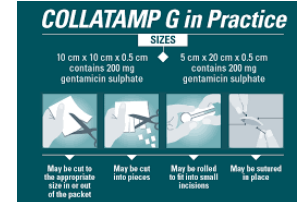
Examples in Pharmaceutical Industry

Biopharmaceuticals:

Monoclonal antibodies, enzymes, peptides, other proteins, vaccines



Special dosage forms: Sublingual tablets, implants



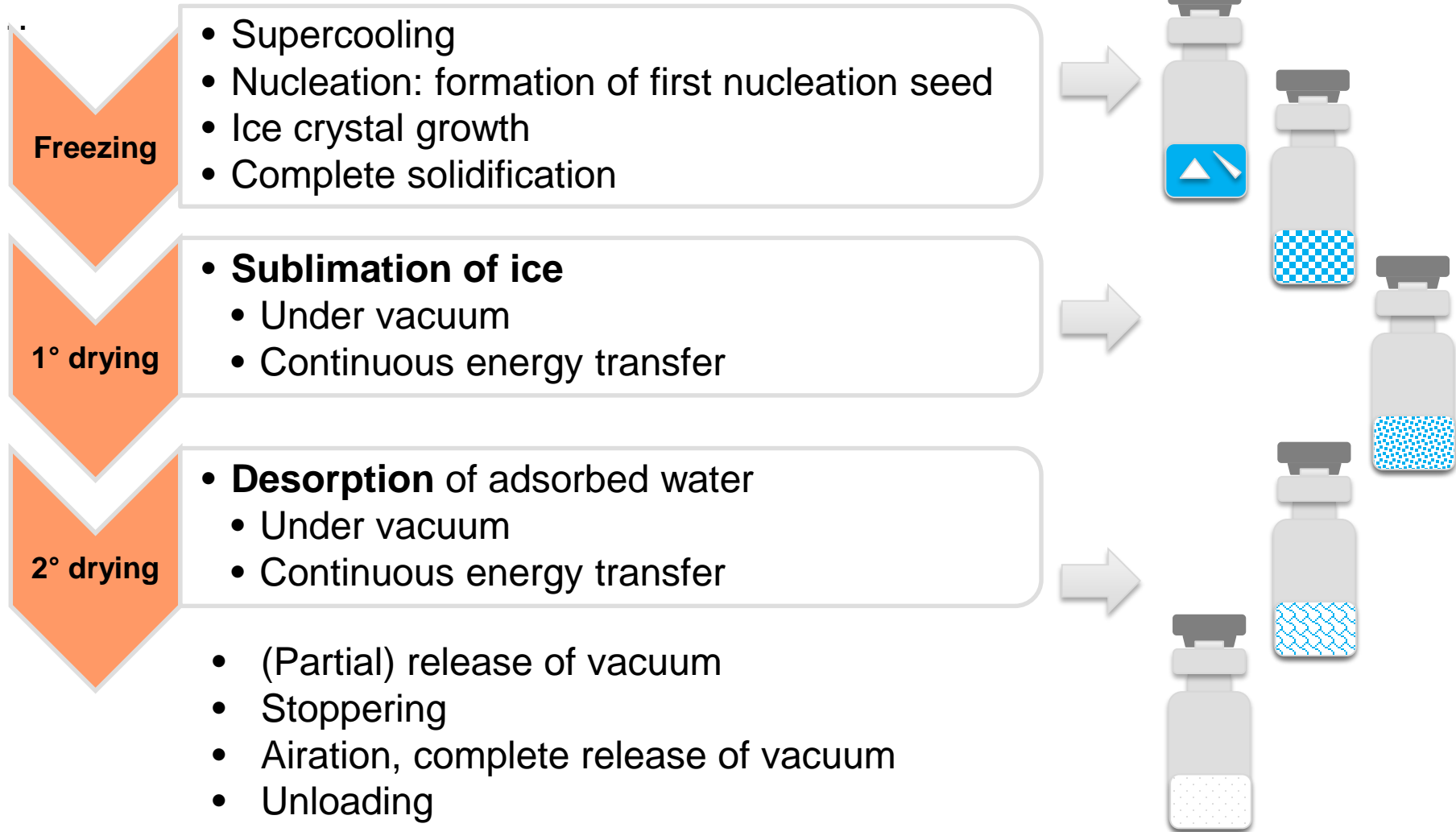
Collatamp® is a lyophilized collagen matrix with the antibiotics Gentamicin

Antibiotics, small molecules, probiotics



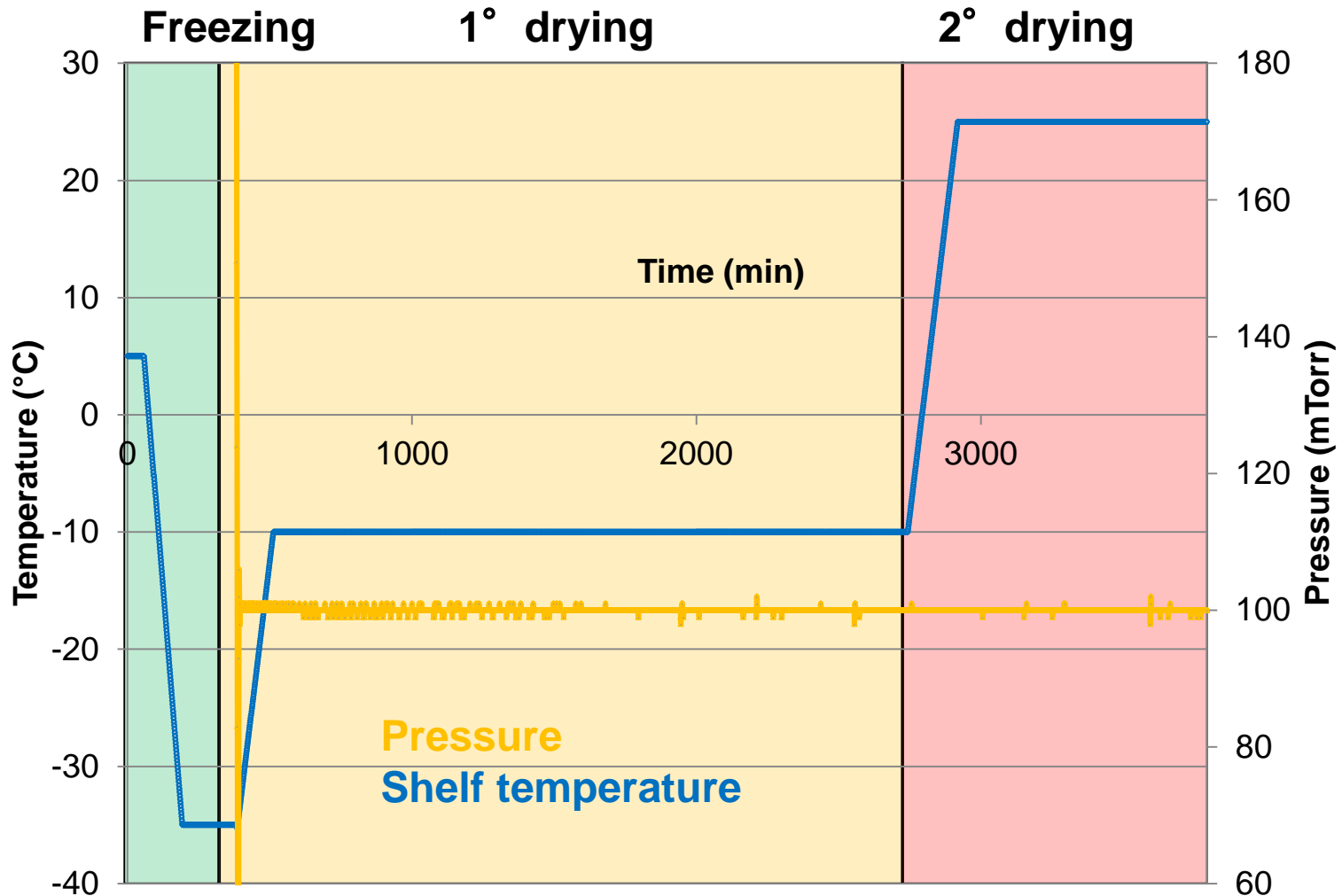


The Freeze drying process



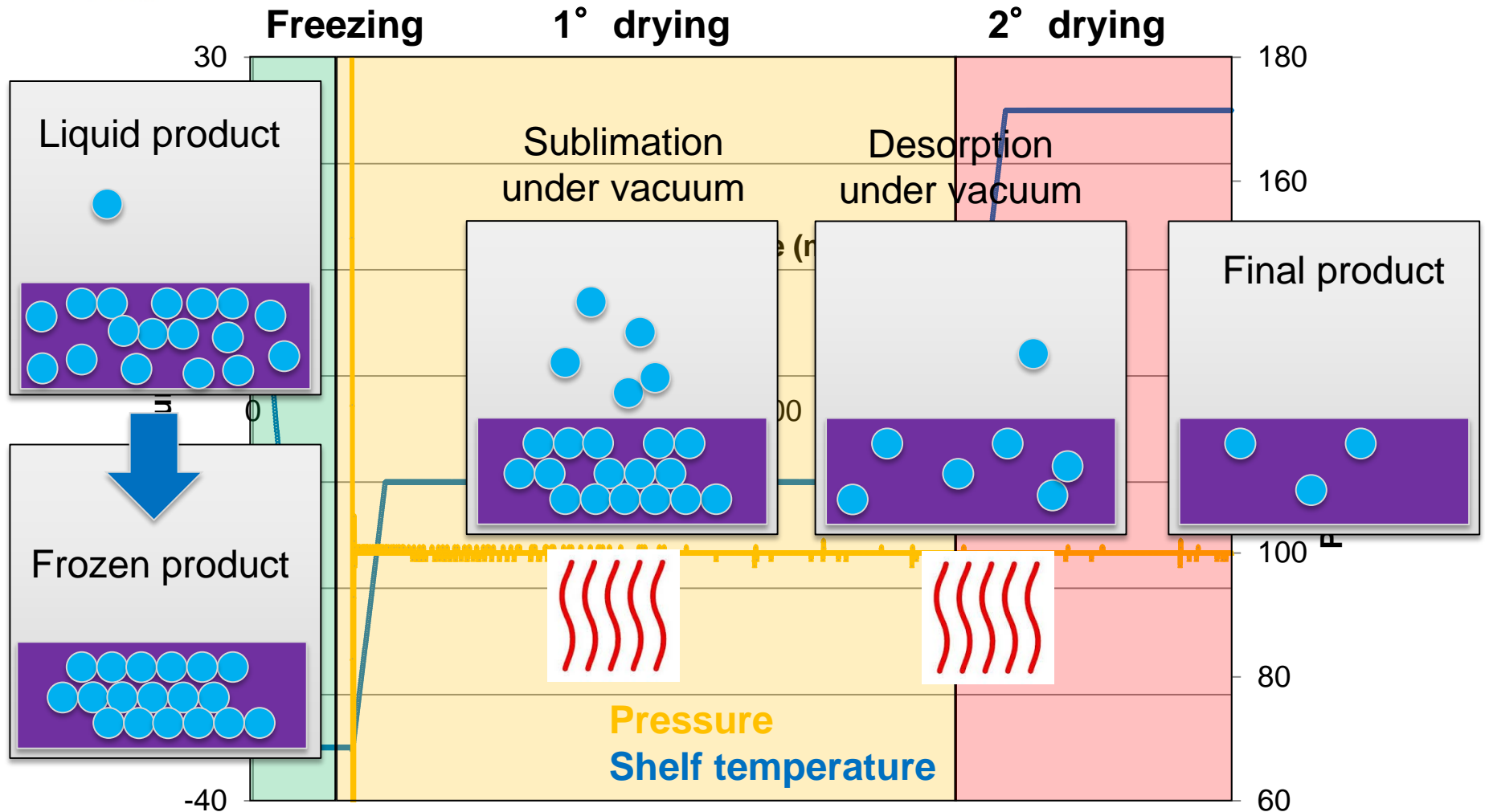


The Freeze drying process



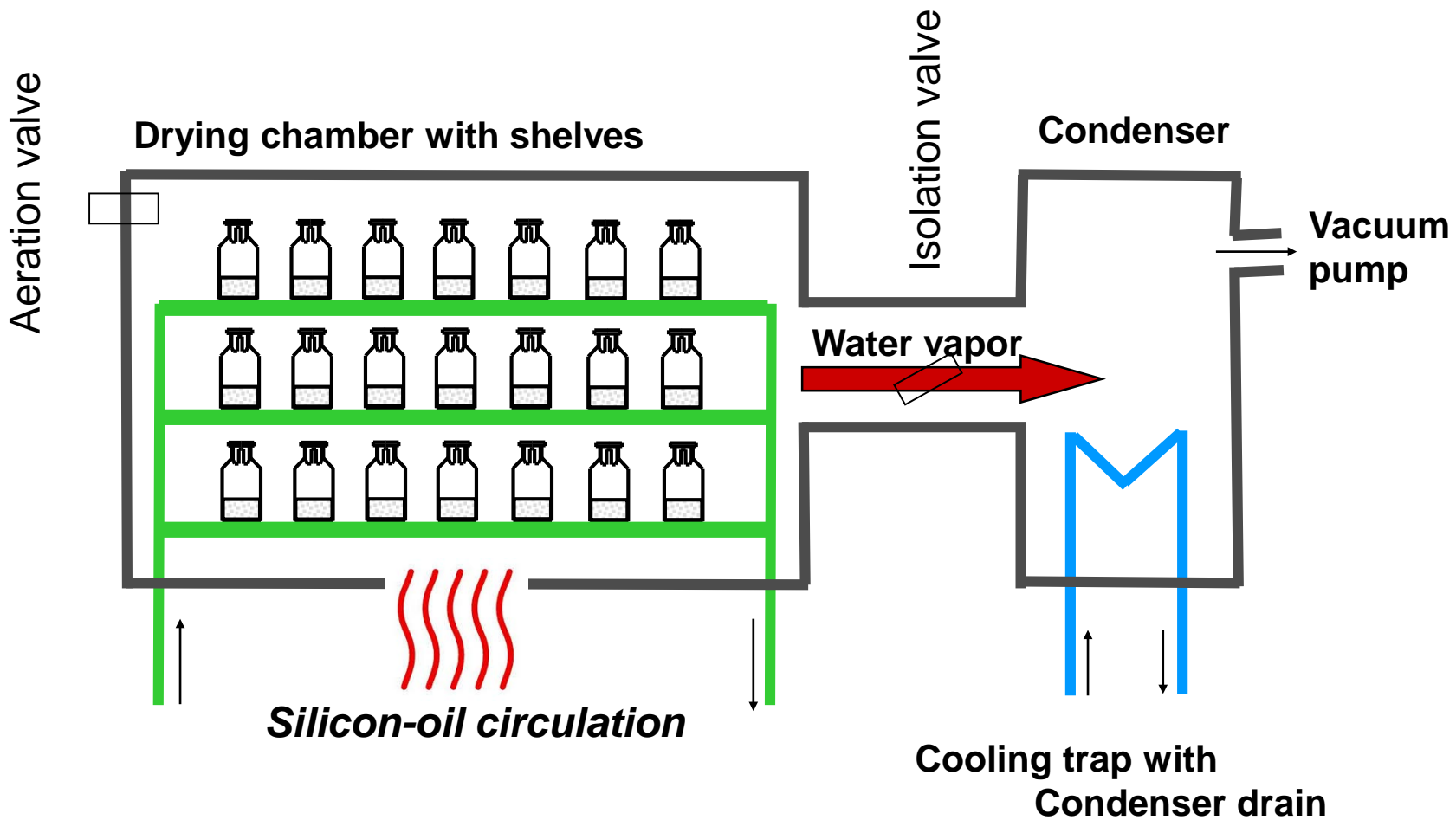


The Freeze drying process



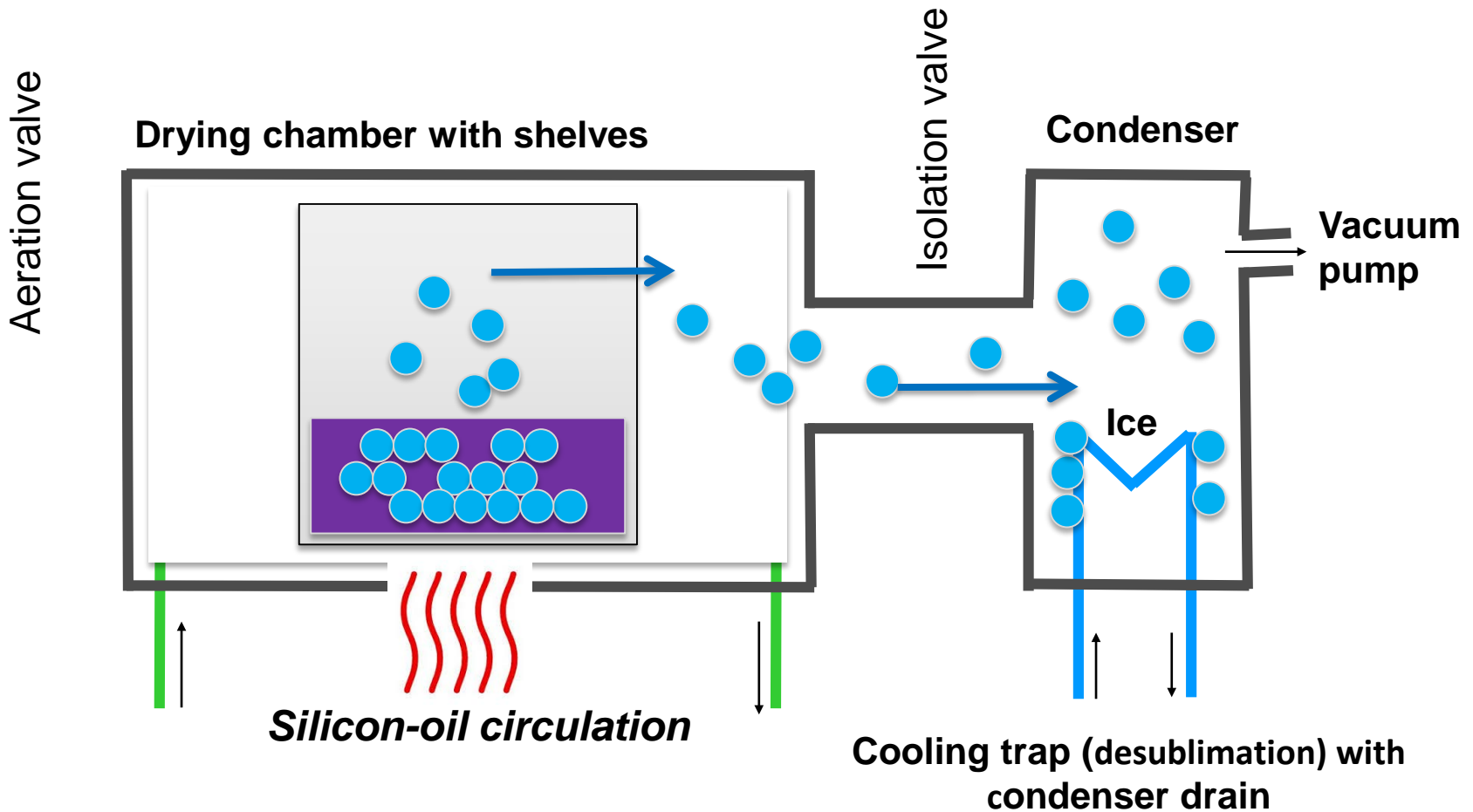


Freeze drying equipment



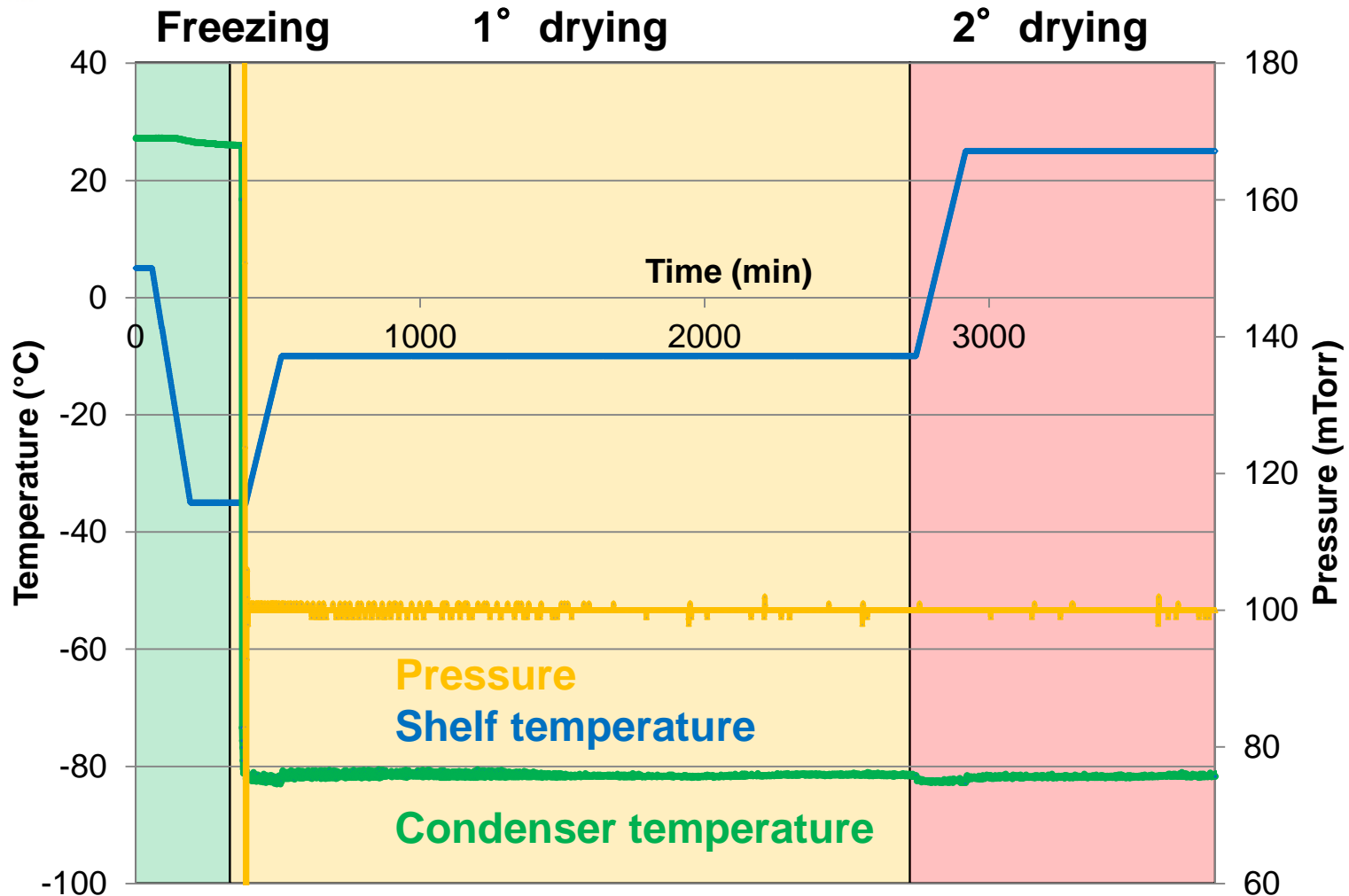


Freeze drying equipment





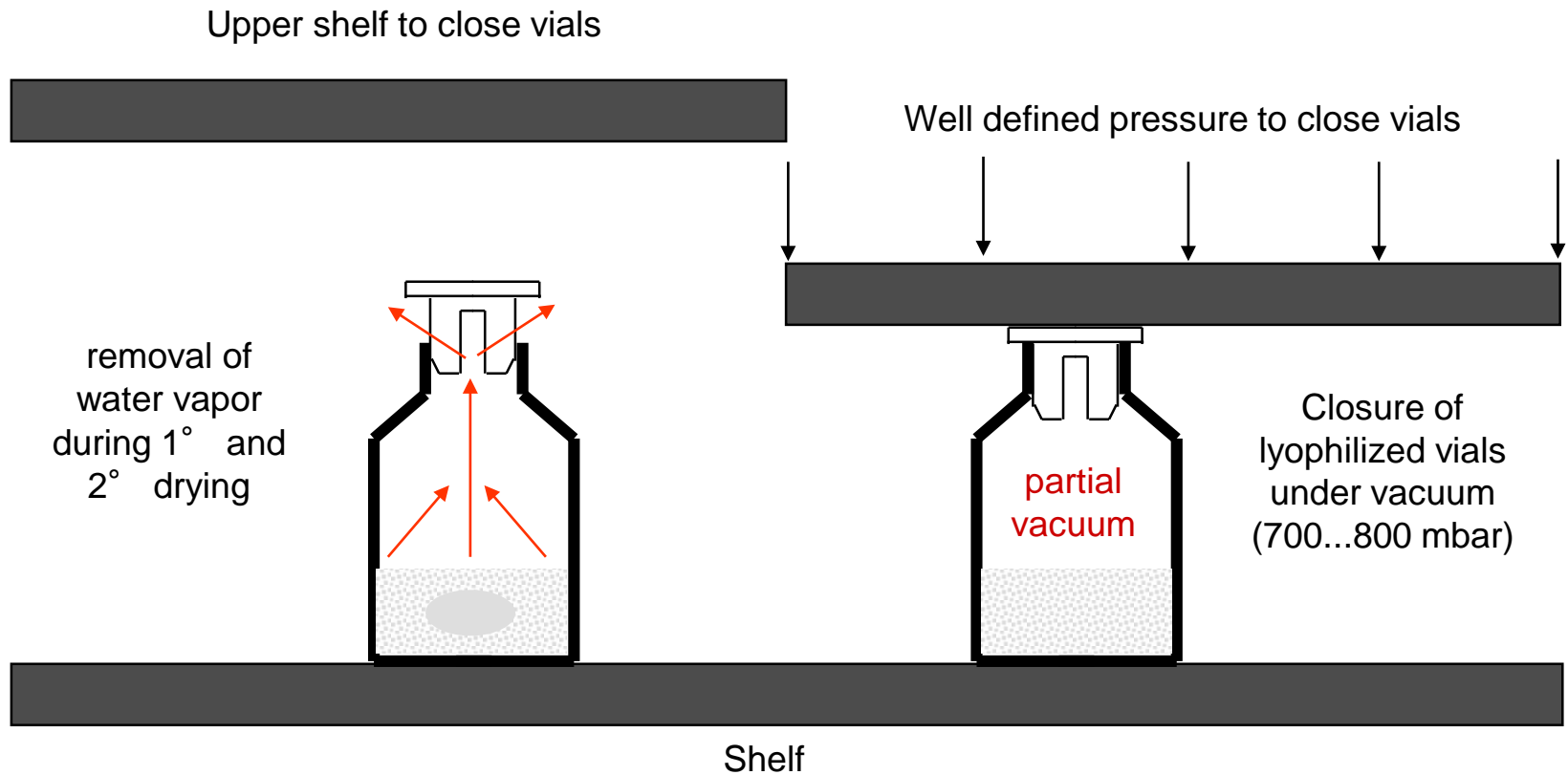
The Freeze drying process





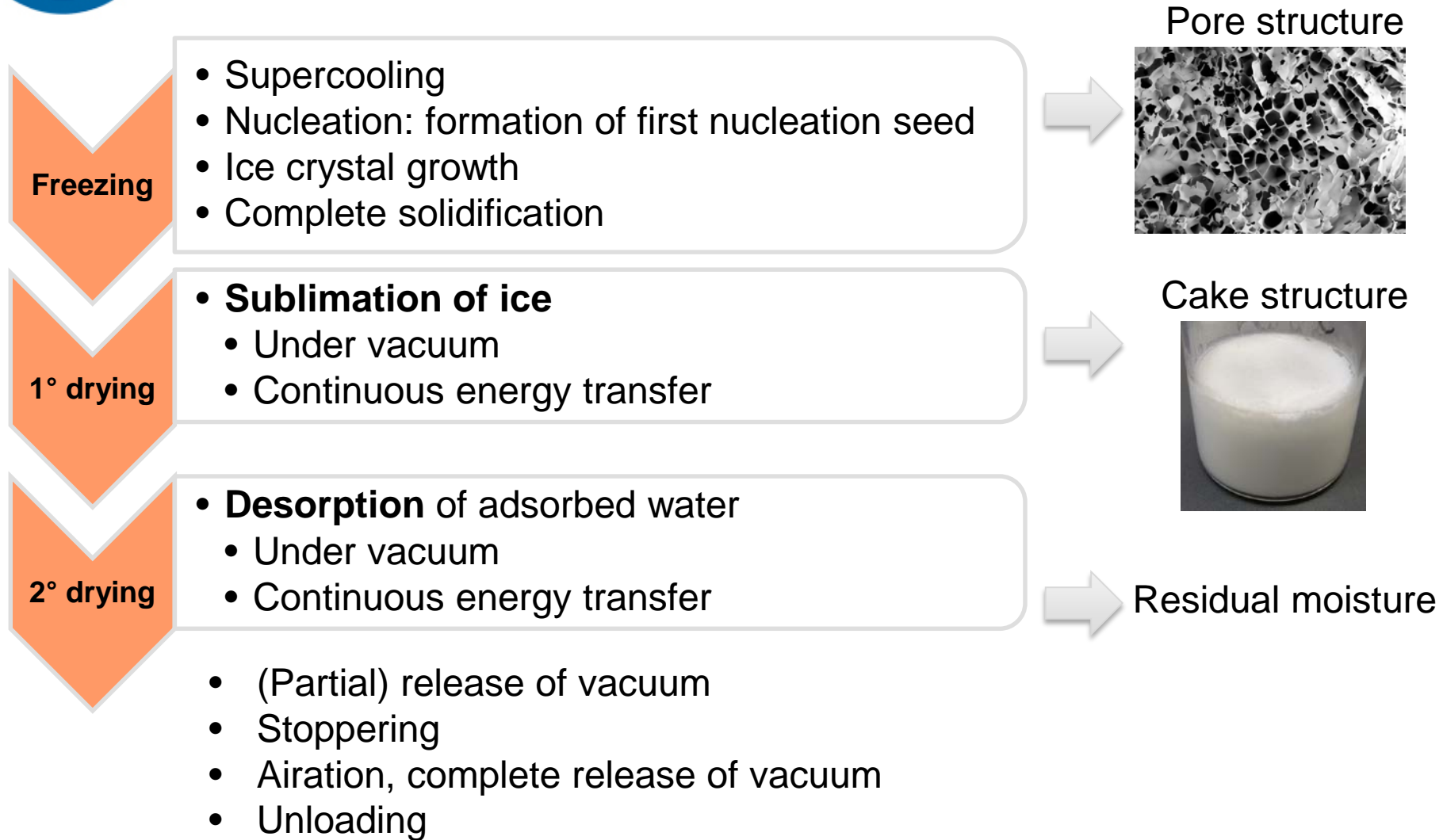
Stopper position

The upper shelf is used to close the vials of the lower shelf in lyophilizers with several shelves.





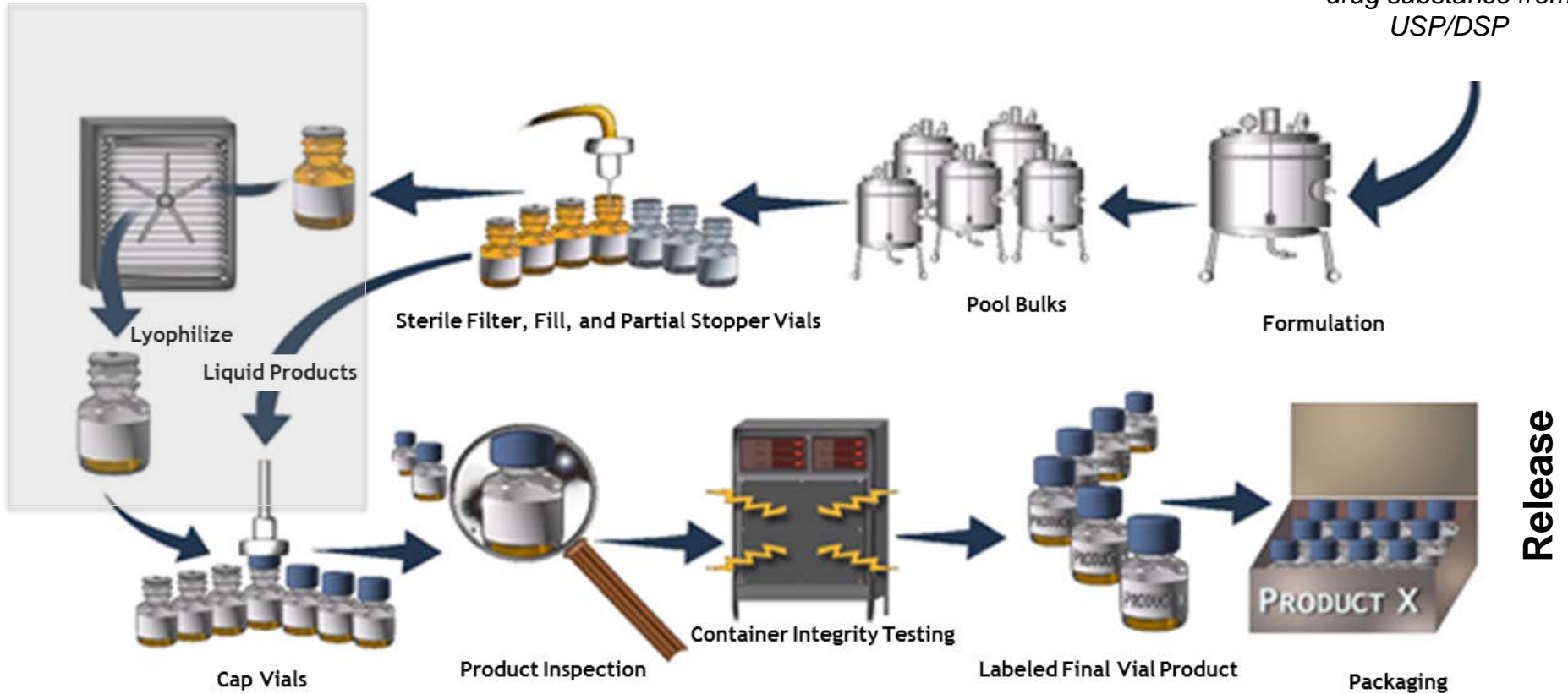
The Freeze drying process





Fill-Finish Manufacturing DP

drug substance from USP/DSP





Pros and Cons for Lyophilization

- **Pro**
 - (in most cases) better stability of e.g. proteins in comparison to liquid formulations
- **Con**
 - Additional process step/ unit operation
 - Time consuming (several days)
 - Energy intensive (>>>90% of constituent are removed) → expensive process!!
 - Batch process (limited batch size)
 - Scale-up and technical transfer needed → highly complex process!
 - For many biologics, the amorphous state has to be maintained in order to have adequate stability
 - Water sensitive (hygroscopic)
 - Handling: Reconstitution step required → Liquid formulations are more convenient/ easier to handle and can be combined with different injection devices