PDA
Parenteral Drug Association

Connecting People, Science and Regulation®

Information for Practical work 1+3

TO DO: Preparation

1. Compounding of formulations
   - Calculation of composition
   - Compounding
2. Filling
3. Stoppering
4. Freezing experiment with distilled water under vacuum to develop a general understanding of the critical temperature

Preparation

Materials:

- active ingredients and excipients (BSA, Sucrose, Mannitol, His, HisHCl-H2O, PS20)
- water for injection
- Schott bottles and beakers; measuring cylinder
- calculator
- scale, magnetic stirrer, spatula
- pH-meter
- pipettes

- 20 mL vials
- lyo stoppers

- thermo couples/ product sensors (2. day)

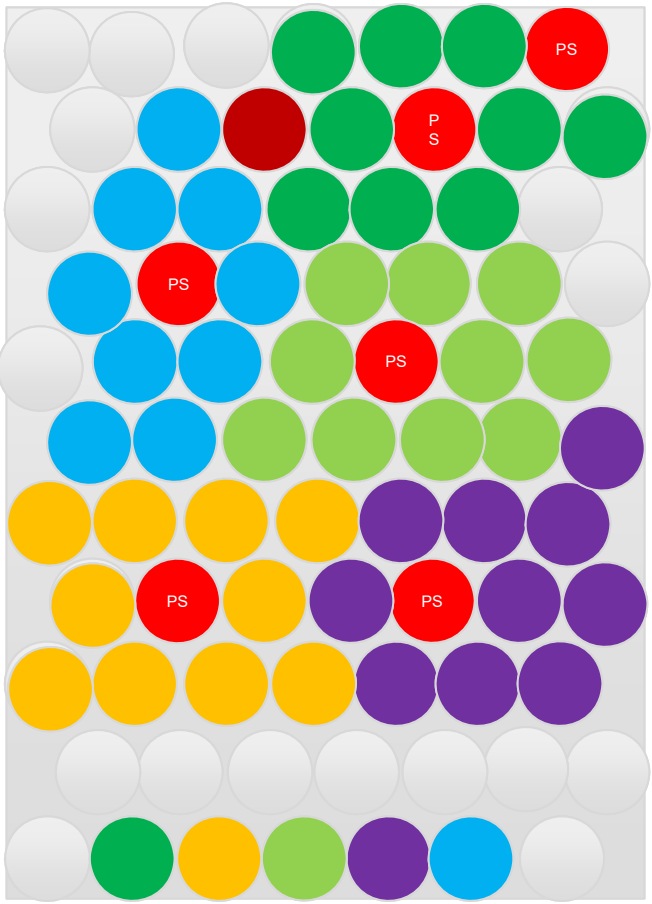
Preparation

Composition of formulations

#	Formulation	BSA	Excipient	Solid content (excipients)	Buffer system	Surfactant	Tg'	Fill volume
1	Formulation 1	25 mg/mL	240 mM Sucrose	~80 mg/mL	20 mM HisHCl pH 6.0	0.02% (w/v) Polysorbat 20	~ -27	10 mL
2	Formulation 2/3	-	240 mM Sucrose	~80 mg/mL			~ -32	10 mL
3								5 mL
4	Formulation 4	-	120 mM Sucrose	~40 mg/mL			~ -32	10 mL
5	Formulation 5	-	220 mM Mannitol	~40 mg/mL			~-1	10 mL

Preparation - Loading

Proposal:



- 3 Lyophilizers
- One shelf per group andlyophilizer will be fully loaded (77 vials)
- Prepare scheme with different formulations including PAT sensors
- Program your receipe

1
2
3
4
5

Complete closed

PS Product sensor

Empty vial

Preparation

1. Calculate the volume needed per formulation depending on the loading scheme. Account for at least 10% overage.
2. Calculate the amount of excipients.
3. Calculate the amount of buffer needed.

As we are 3 groups – please consolidate and discuss who is preparing what and how much!

Preparation

working sheet

Composition of formulations:

Formulation #	Number of vials	Fill volume	Total volume needed	Total volume prepared* (L)	BSA concentration (mg/mL)	BSA (g)	Excipient concentration (mM)	Excipient concentration (g/L)	Excipient (mg)	Tensid + buffer system
1	_____	10 mL	_____	_____	25 mg/mL	_____	240 mM Sucrose	_____	_____	20 mM HisHCl pH 6.0: + 0.02% (w/v) PS20
2	_____	10 mL	_____	_____	-	-	240 mM Sucrose	_____	_____	
3		5 mL			-	-				
4	_____	10 mL	_____	_____	-	-	120 mM Sucrose	_____	_____	
5	_____	10 mL	_____	_____	-	-	220 mM Mannitol	_____	_____	
Total										_____ _____ _____

* Include 10% loss

Molar Mass:
Sucrose 342.3 g/mol
Mannitol 182.2 g/mol

Buffer receipt 1L:
- 2.196 g of His-HCl Monohydrat
- 1.477 g of Histidin, freie Base
- Ad 1 L

Preparation

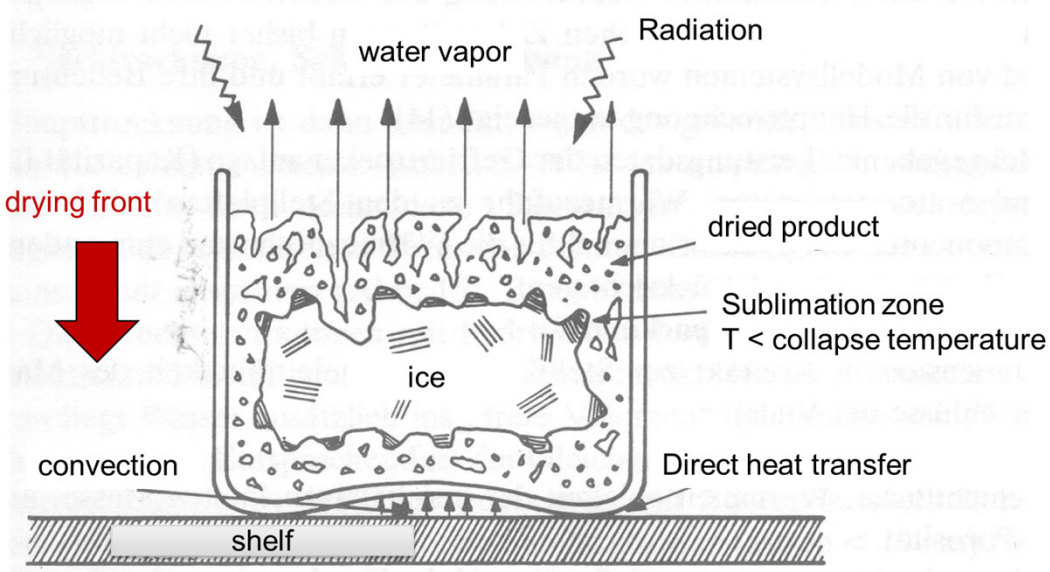
1. Prepare the buffer and add the surfactant.
2. Compound the formulations by using the prepared buffer system
3. Fill the formulations into the glass vials
4. Position the stoppers to allow for sublimation
5. Position the thermo couples

TO DO: @ the lyophilizer

1. Loading of the shelves
2. Positioning of the thermo couples
3. Programming of the lyophilization cycle
4. Start of the lyophilization program

Placement of thermo couples

For the correct position of a thermo couple / sensor to monitor product temperature, the tip of the sensor needs to just above the middle of the vial bottom.



PAT

PAT	Epsilon 2-DLSC+ Lyo I *(controlled nucleation)*	Epsilon 2-DLSC+ Lyo II	Epsilon2-4LSC+ Lyo III
Pirani	X	X	X
MKS	X	X	-
Komparative Druckmessung	X	X	-
PT100	X	X	X
WTM+	X	X	X
LyoRx	X	X	X
Lyobalance	X	(X)	-
LyoCam	X	X	-
ΔP/Δt	X	X	-