Information to Practical Work
1 + 3

PDA EU
Freeze – Drying In Practice

Dr. Julian Lenger

Head of Laboratory in Parenteral Drug Development at Bayer AG;

julianh.lenger@gmail.com

24 – 28 October 2022
Martin Christ
Osterode am Harz, Germany

Adapted from slides originally created and kindly provided by PD Dr. Andrea Allmendinger

PDA Parenteral Drug Association

CONNECTING PEOPLE SCIENCE AND REGULATION®

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)

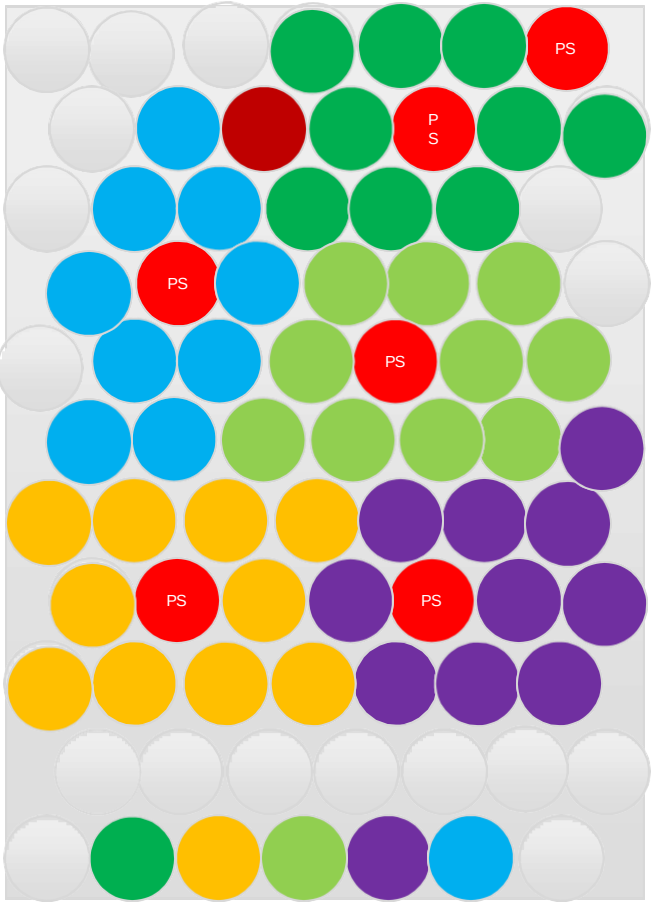
Preparation

Composition of formulations

#	Formulation	BSA	Excipient	Solid content (excipients)	Buffer system	Surfactant	T_g' / T_{eu}	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 / 3 groups
- One shelf (77 vials) will be fully loaded per group and lyophilizer
- Prepare your own loading scheme with different formulations including PAT sensors

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 with water

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 and stopper them completely

   in the afternoon:

4. Position the stoppers to allow for sublimation (semi-stoppered position)
5. Position the thermo couples
6. Load the lyophilizer
7. Program your recipe (Theory 3) and install/connect all PAT tools that you would like to use
8. Start the program and see the magic happen ☺

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.