



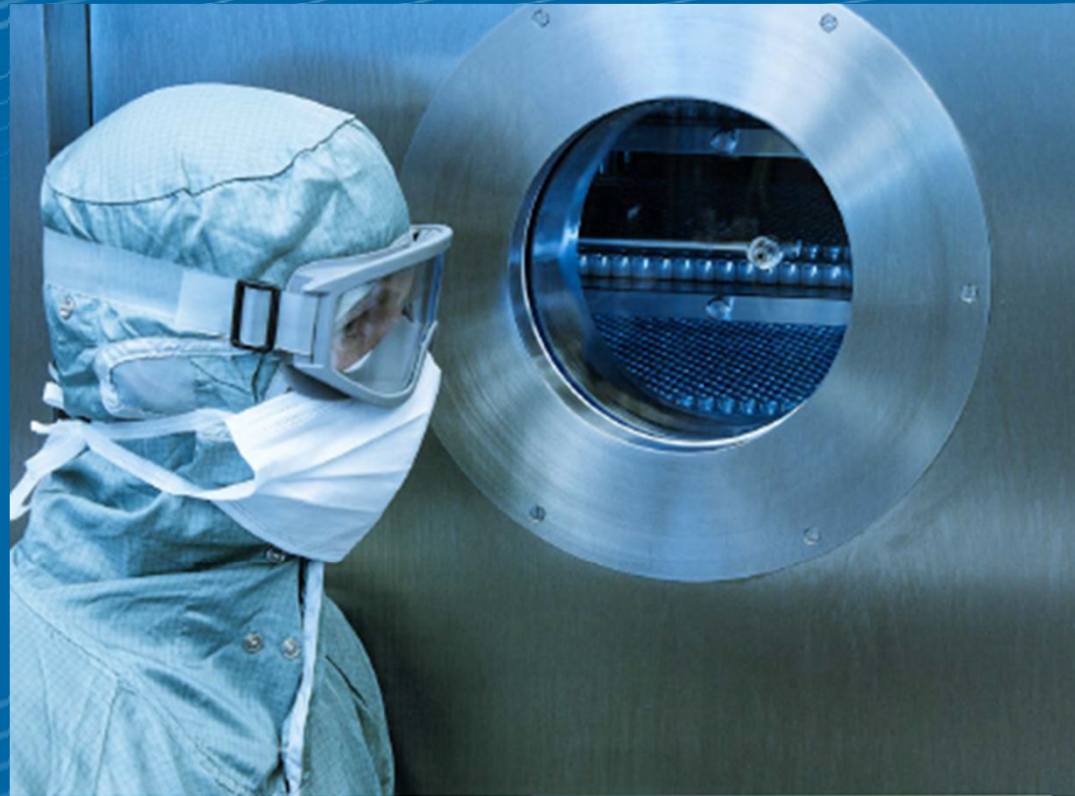
Connecting People, Science and Regulation®

Information to Practical work 1+3

Dr. Andrea Allmendinger

*Late-stage Pharmaceutical and
Processing Development
Hoffmann-La Roche, Basel*

andrea.allmendinger.aa1@roche.com



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2019 PDA EUROPE TRAINING

Freeze Drying in Practice



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
- sterile filters and vacuum pump if available

- 20 mL vials
- lyo stoppers

- thermo couples/ product sensors (2. day)



Preparation

Composition of formulations

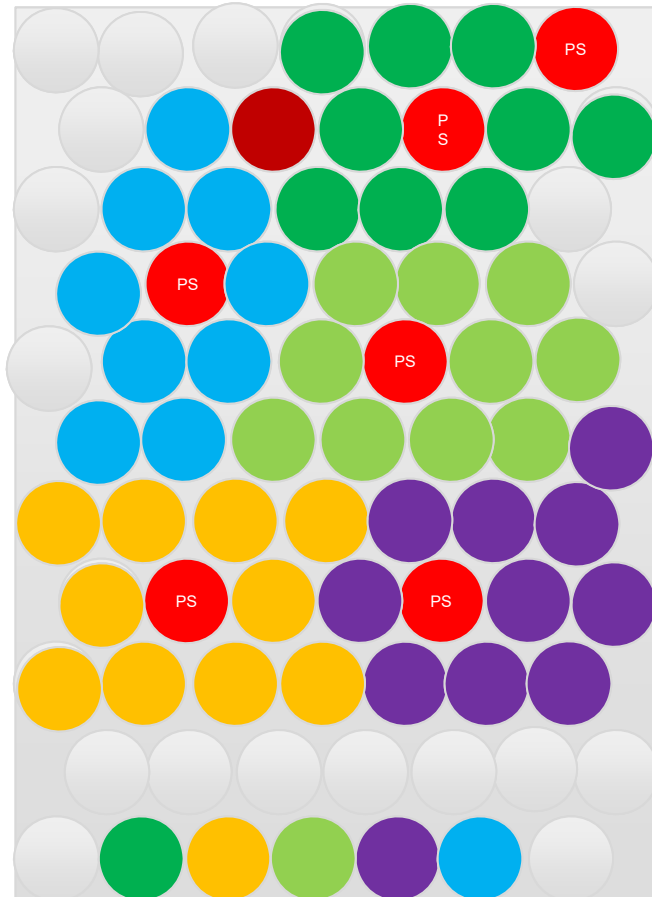
#	Formulation	BSA	Excipient	Solid content (excipients)	Buffer system	Surfactant	Tg'	Fill volume
1	Formulation 1	25 mg/mL	240 mM Sucrose	~80 mg/mL	20 mM HisHCl pH 6.0	0.02% (w/v) Polysorbat 20	~ -27	10 mL
2	Formulation 2/3	-	240 mM Sucrose	~80 mg/mL			~ -32	10 mL
3								5 mL
4	Formulation 4	-	120 mM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



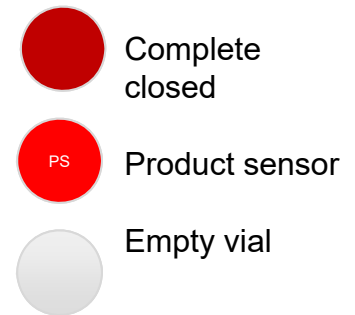
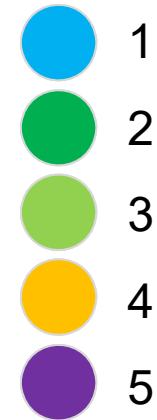


Preparation - Loading

Proposal:



- 3 Lyophilizers / 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





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 and filter
3. Fill the formulations into the glass vials and stopper them completely
(next day:)
4. Position the stoppers to allow for sublimation
5. Position the thermo couples
6. Load the lyophilizer
7. Program your recipe and install/connect all PAT tools that you would like to use
8. Start the 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 be just above the middle of the vial bottom.

