subject to change – 16 Apr 2018

Monday, 23 April 2018

12:00 **Reception and Welcome Snack**

12:30 INTRODUCTION
- **Collection and clustering of the questions contributed by the participants**

13:00 THEORY 1 – INTRODUCTION TO FREEZE DRYING PROCESSES
- **Why lyophilization?**
- **History and Development**
- **Examples in daily life and pharmaceutical industry**
- **The freeze drying process**
- **Freeze drying equipment**
- **Pros and Cons for Lyophilization**

13:45 THEORY 2 - PRINCIPLES OF THE FREEZE DRYING PROCESS
- **Basic principles of freeze drying processes**
  - Physical understanding
  - Critical process parameters
  - Controlled nucleation
- **Primary packaging components**
- **Solid state characterisation of lyophilisates**
- **Development and composition of a (biological) formulation**

15:15 **Excursus 1: Drying of tert-butyl alcohol**

15:35 **Coffee Break**

15:50 PRACTICE 1 - PREPARATION OF SOLUTIONS
- **Compounding of formulations**
  - Calculation of composition
  - Compounding
- **Filling**
- **Stoppering**
- **Freezing experiment with distilled water under vacuum to develop a general understanding of the critical temperature**

18:00 **Transfer to the Networking Dinner**

18:30 **Networking Dinner**

21:00 **Return to the recommended Hotels**

Tuesday, 24 April 2018

08:30 **Transfer from the recommended hotels to Martin Christ facility**

09:00 **Recapitulation and Summary of Day 1**

09:10 THEORY 3 - DEVELOPMENT OF A FREEZE DRYING PROCESS

- **Development of a lyophilization cycle**
  - Which are the most important parameters?
  - How to choose them?
  - What happens if they are not chosen adequately?
- **Simulation tools**
- **Finalization of cycles**

10:30 **Coffee Break**

10:45 THEORY 4 - PROCESS CONTROL TOOLS

- **Thermal resistance measurement (Lyo-RX)**
- **Comparative pressure measurement (Pirani/capacitive pressure measurement)**
- **Barometric temperature measurement (BTM/MTM)**
- **Wireless temperature measurement (WTM)**
- **Desorption rate measurement (DRM)**
- **Conductance sensor**
- **Inline camera (LyoCam)**

11:45 PRACTICE 2: PROGRAMMING

- **Programming the freeze dryer with the programs developed in Theory 3**

12:45 **Lunch Break**

13:45 PRACTICE 3: FREEZING BEHAVIOR

- **Loading of the shelves**
- **Positioning of the thermo couples**
- **Programming of the lyophilization cycle**
- **Start of the lyophilization program**
- **Introduction to the lyocam technology**

14:15 PRACTICE 4:

- **Introduction to the LyoCam technology**
- **Play-back and discussion of prepared/available video sequences**
- **Discussion on the correlation of the video sequences with the process parameters using the process graphs**
- **Time lapse mode for identifying process advancement**

15:00 **Coffee Break**

15:30 THEORY 5 - OPERATING PRINCIPLES OF THE FREEZE DRYER

- **Overview of different operating and construction principles of freeze dryers**
- **Construction principle of the freeze dryer and its device modules**
- **Performance figures (port sizes, condenser sizes, evacuation times)**
- **Chamber system**
- **Cooling & vacuum systems**
- **Filter systems**
- **CIP/SIP**
- **Interaction of the device modules in the freeze drying process**

17:00 **Exkursus 2: Controlled Nucleation**

17:20 PRACTICE 5 - A GLANCE AT FREEZE DRYERS

- **Discussion of the current status of the process**
- **What is evident/what is not yet evident**

18:00 **Transfer from Martin Christ facility to the recommended hotels**

Wednesday, 25 April 2018

8:30 **Transfer from the recommended hotels to Martin Christ facility**

9:00 **Recapitulation of Key Learnings from Day 2**

9:10 PRACTICE 6 - TOUR OF THE PRODUCTION ROOMS OF MARTIN CHRIST

- **Introduction to the different size classes of freeze dryers**
- **Introduction to the functional modules of the freeze dryer**
- **Visualization of the basic analogy of the functional modules across the size classes**
- **Explanation of the step-by-step production process for freeze dryers**

10:00 THEORY 6 - LYO QUALIFICATION

- **Explanation of the sequence DQ-RA-IQ-OQ-PQ**
- **Measures for maintaining the qualified state**

10:45 **Coffee Break**

11:00 PRACTICE 7 - INTRODUCTION TO THE GENERAL ORDER OF EVENTS IN OPERATION

- **Brief explanation of all workstations**
- **Explanation and instruction on the logistics**

11:30 PRACTICE 8

- **Discussion of the current status of the process in the freeze dryer**

12:00 **Lunch Break**

13:00 PRACTICE 9: WORKSTATION OPERATION SEQUENCE 1

- **Calibration of pressure sensor/vacuum sensor**
- **Calibration of temperature sensor**
- **Shelf temperature mapping**
- **Roughness measurement**

13:45 CONTINUATION PRACTICE 9: WORKSTATION OPERATION SEQUENCE 2

- **Calibration of pressure sensor/vacuum sensor**
- **Calibration of temperature sensor**
- **Shelf temperature mapping**
- **Roughness measurement**

14:30 CONTINUATION PRACTICE 9: WORKSTATION OPERATION SEQUENCE 3

- **Calibration of pressure sensor/vacuum sensor**
- **Calibration of temperature sensor**
- **Shelf temperature mapping**
- **Roughness measurement**

15:15 **Coffee Break**

15:30 CONTINUATION PRACTICE 9: WORKSTATION OPERATION SEQUENCE 4

- **Calibration of pressure sensor/vacuum sensor**
- **Calibration of temperature sensor**
- **Shelf temperature mapping**
- **Roughness measurement**

16:30 PRACTICE 10 - MAINTENANCE AND FAULT CORRECTION

- **Introduction to the most frequently occurring faults**
  - Diagnosis
  - Most probable causes
  - Correction
- **Introduction to a preventative maintenance concept**
- **Presentation of examples of defective components with explanation of the causes**

17:30 THEORY 7 - CIP & SIP

- **Inspection of CIP & SIP systems**
- **Cleaning validation**
- **Sterilization qualification**
- **Turn-around concept**

18:15 PRACTICE 11

- **Discussion of the current status of the process in the freeze dryer**

18:45 **Transfer from Martin Christ facility to the recommended hotels**

Thursday, 26 April 2018

8:30	**Transfer from the recommended hotels to Martin Christ facility**
9:00	**Recapitulation of Key Learnings from Day 3**
9:20	PRACTICE 12 • **Simulation of major faults with freeze driers** • **Diagnosis (and simulation) of the correction of major faults**
10:20	**Coffee Break**
10:40	PRACTICE 13 • **Explanation of conductance sensor** • **Inspection and explanation of the CIP/SIP-functional modules in an industrial freeze dryer** • **"Contamination" of a freeze dryer with riboflavin solution** • **Start of the CIP cycle**
13:00	**Lunch Break**
14:00	THEORY 8 • **Introduction to the functioning and operation of the RM measuring instrument** • **Presentation of theory, function and purpose of the most important analysis techniques for lyophilizates** • **Introduction to the measurement of residual moisture**
15:00	**Coffee Break**

15:20	THEORY 9 – ANALYTICAL CHARACTERIZATION OF LYOPHILISATES
	• **Product attributes for designing lyophilization cycles**
	  • Differential scanning calorimetry
	  • Freeze drying microscopy
	• **Solid state characterization after lyophilization**
	  • Residual moisture (Karl Fischer, NIR)
	  • Reconstitution time
	  • Thermodynamic state (Xray powder diffraction)
	  • Specific surface area (BET)
	  • Cake appearance at different levels (visual inspection, 3D scanning, PDMS embedding, SEM, µCT)

16:20	PRACTICE 14 • **Discussion of the current status of the process in the freeze dryer** • **Visual control – examples**
17:20	**Transfer from Martin Christ to dinner location**
18:00	**Farewell Dinner**
21:00	**Transfer from dinner location to the recommended hotels**

Friday, 27 April 2018

8:30	**Transfer from the recommended hotels to Martin Christ facility**
9:00	PRACTICE 15 • **Unloading the freeze dryer** • **Evaluation of the process chart** • **Determination of reconstitution time** • **Visual Inspection** • **Assessment of the different results**
10:00	**Q&A and conclusions**
12:00	**End of Course**

Faculty

Andrea Allmendinger, *PhD, Senior Scientist, Hoffmann-La Roche Basel*

Andrea Allmendinger is a pharmacist by training and conducted her studies at the University of Heidelberg in Germany and at the University College London. She holds a PhD in Pharmaceutical Technology from the University of Basel. Andrea joined Hoffmann-La-Roche Basel in 2010, where she currently holds the position as Senior Scientist in the Late-stage Pharmaceutical and Processing Development Department for parenteral products. Andrea is specialized in highly concentrated monoclonal antibody formulations and in particular in the development of freeze dried, parenteral formulations, as well as process development, optimization and transfer of lyophilization cycles. In addition to her role at Roche, she is lecturer at the University of Freiburg in the department of Pharmaceutical Technology and Biopharmacy since 2015.

Klaus Hudel, *PhD, Business Development Manager, Martin Christ GmbH*

After his studies of chemical engineering at the University of Dortmund, Klaus held a position as test engineer in a public water and waste association. His following position at the well-known German RWTH Aachen University consisted in practical industrial projects. After achieving his PhD in engineering about a thermal treatment topic, he moved to the appropriate industry where he worked as project engineer for big scale drying equipment. For almost 20 years now, Klaus works for in Martin Christ Gefriertrocknungsanlagen GmbH. In his current position as business development manager he is not only responsible for market perspectives and key customer relations, but is also busy in seminars and workshops about freeze drying.

Sascha Pfeiffer, *Managing Director, Lyo Engineering*

Sascha Pfeiffer is a Pharma Quality Engineer with over 10 years of experience in Pharma Engineering in the area of API Fill Finish. Sascha founded Lyo Engineering in 2013 and holds the role as Managing Director. Lyo Engineering is a Consulting Company in the Areas Management, Freeze Dryer Process Engineering and Quality Issues (Quality Assurance, Qualification and Validation). Sascha is specialized in Quality Assurance Engineering and in technical Transfers, as well as plant process optimization.

Additional employees of Martin Christ Gefriertrocknungsanlagen GmbH are operating as trainers and supporting staff for the practical exercises.