

Recap day 1

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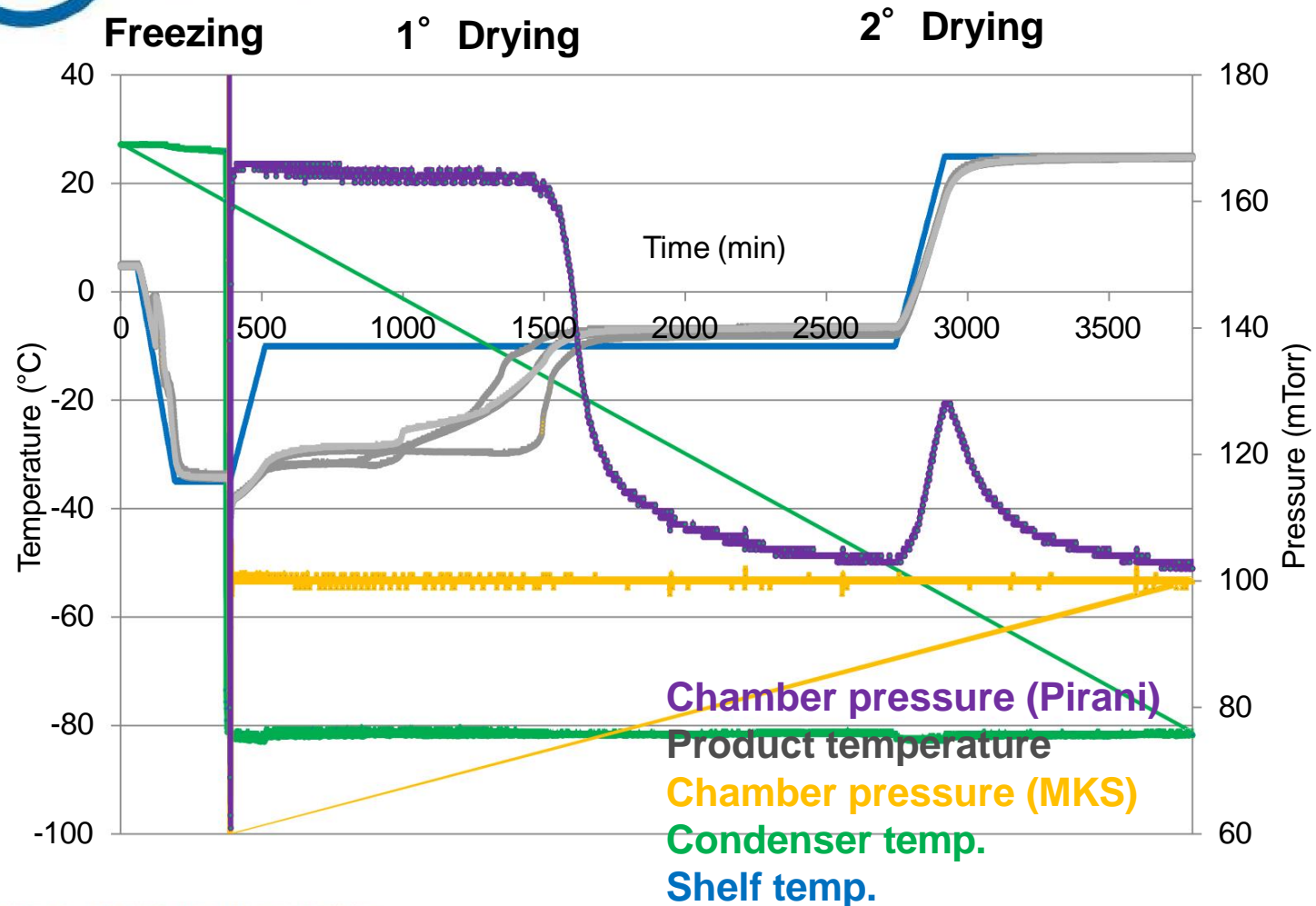
Freeze-drying in practice

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The freeze-drying process at a glance



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Development of a lyophilization cycle

1. Shelf temperature

- 1°drying
- 2°drying

2. Chamber pressure

3. Drying time (isothermal hold time) ← **PAT tools!**

4. Ramp time



Lyophilization Program

**working sheet
Conservative**

Regulation of vacuum: Pirani MKS

Product assumptions: $T_g' = -32\text{ }^\circ\text{C}$;
drying safely **below** T_g' ; **8%** solute conc.
Target $T_p = -34\text{ }^\circ\text{C}$

Process step	Manual mode: Loading (Pre-cooling)	Freezing	Freezing	Freezing	Freezing	1° drying	1° drying	1° drying	2° drying	2° drying	Manual mode: stoopering
Time (hh:mm)		0:15	01:00	0:45	03:30	0:01	0:18	49:00	3:55 (0.2K/min)	06:00	
Shelf temp. (°C)	20	5	5	-40	-40	-40	-22	-22	25	25	
Vacuum (mbar)	off	off	off	off	off	0.14	0.14	0.14	0.14	0.14	750
Safety pressure (mbar)	off	off	off	off	off	0.26	0.26	0.26	0.26	0.26	
ΔT shelf (°C)		off	off	off	off	off	off	off	off	off	
ΔT product (°C)		off	off	off	off	off	off		off	off	
LyoControl Rx (%)		off	off	off	off	off	off	off	off	off	
camera interval (min)		15	60	1	5	10	10	10	10	60	



Lyophilization Program

**working sheet
Regular**

Regulation of vacuum: Pirani MKS

Product assumptions: $T_g' = -32^\circ\text{C}$;
drying around T_g' ; 8% solute conc.
Target $T_p = -32^\circ\text{C}$

Process step	Manual mode: Loading (Pre-cooling)	Freezing	Freezing	Freezing	Freezing	1° drying	1° drying	1° drying	2° drying	2° drying	Manual mode: stoopering
Time (hh:mm)		0:25	01:00	0:35	03:30	0:01	0:25	30:00?*	03:20 (0.2 K/min)	06:00	
Shelf temp. (°C)	20	-5	-5*	-40	-40	-40	-15	-15	25	25	
Vacuum (mbar)	off	off	off	off	off	0.096 or 0.1 mbar	0.096 or 0.1 mbar	0.096 or 0.1 mbar	0.096 or 0.1 mbar	0.096 or 0.1 mbar	750
Safety pressure (mbar)	off	off	off	off	off	0.26	0.26	0.26	0.26	0.26	
ΔT shelf (°C)		off	off	off	off	off	off	off	off	off	
ΔT product (°C)		off	off	off	off	off	off		off	off	
LyoControl Rx (%)		off	off	off	off	off	off	off	off	off	
camera interval (min)		15	60	1	5	10	10	10	10	60	

*Controlled Nucleation after 1h hold time, hold time 15min, nuc at 7 mbar

**Comparative pressure measurement (10-15% difference)



Lyophilization Program

working sheet
Aggressive

Regulation of vacuum: Pirani MKS

Product assumptions: $T_g' = -27^{\circ}\text{C}$;
drying **above** T_g' ; **8%** solute conc.
Target $T_p = -25^{\circ}\text{C}$ or -23°C

Process step	Manual mode: Loading (Pre-cooling)	Freezing	Freezing	Freezing	Freezing	1° drying	1° drying	1° drying	2° drying	2° drying	Manual mode: stoopering
Time (hh:mm)		0:15	01:00	0:45	03:30	0:15	00:60	15:00?*	00:05	06:00	
Shelf temp. (°C)	20	5	5	-40	-40	-40	20	20	25	25	
Vacuum (mbar)	off	off	off	off	off	0.14	0.14	0.14	0.14	0.14	750
Safety pressure (mbar)	off	off	off	off	off	0.26	0.26	0.26	0.26	0.26	
ΔT shelf (°C)		off	off	off	off	off	off	off	off	off	
ΔT product (°C)		off	off	off	off	off	off		off	off	
LyoControl Rx (%)		off	off	off	off	off	off	off	off	off	
camera interval (min)		15	60	1	5	10	10	10	10	60	