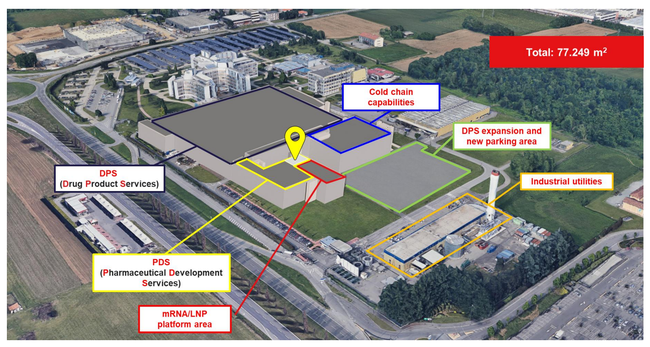
From Conventional Batch Lyophilizer to Continuous Spin-Freeze-Drying Technology: Lyophilized Drug Product in hours instead of days

Emanuela Turdo[1], Fabio Selis[1], Edoardo Iaconelli[1], Joris Lammens[2], Thomas De Beer[2], Giuseppina Salzano[1]

[1] *Formulation and Analytical Development Laboratory at Patheon, part of Thermo Fisher Scientific, Monza, Italy*
[2] *RheaVita, Ghent, Belgium*

TFS Monza Campus



TFS Monza PDS Formulation & Analytical Development Laboratory Services and Tailor-Made Solutions

Early Stage	Middle Stage
Pre-formulation Studies & Prototype	Product Contact Part Compatibility & In-Use Studies
Familiarization Study & Compounding Design	Lyophilization Cycle Robustness (DoE)
Purification/Filtration Design	Formulation Robustness (DoE)
Lyophilization Cycle Development & Scale-up	Holding Time Studies
Fill Volume Determination	Freeze-thaw Studies
Spiking Study (oxidant)	Pumping Recirculation Studies
Terminal Sterilization Study	Mixing Study
Toxicological Batch Manufacturing	Vials to PFS Transition Study



Purpose

Continuous spin freeze-drying integrates spin-freezing, primary drying, and secondary drying into a fully continuous process. During spin-freezing, vials are rotated under a controlled gas flow, creating a thin and homogeneous frozen layer along the vial wall. This configuration enhances heat and mass transfer, accelerates sublimation, and has the potential to substantially reduce freeze-drying cycle times while maintaining product quality.
In this context, the **R&D Formulation and Analytical Development Laboratory of Thermo Fisher Scientific (Monza, Italy)** investigated the application of the **RheaVita continuous lyophilization technology** to a challenging formulation, in comparison with a conventional lyophilizer.

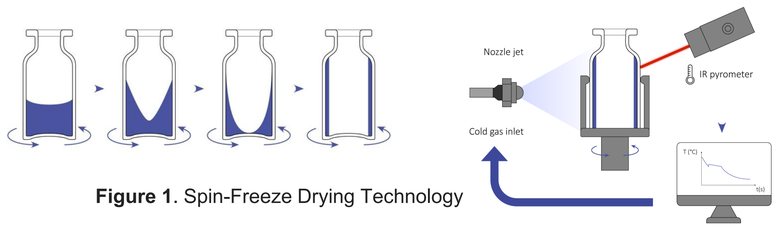


Figure 1. Spin-Freeze Drying Technology

OBJECTIVES OF THE STUDY

- **Accelerating lyophilized product manufacturing**
- **Improving the product-specific CQAs**

Methods

A comparative study was performed between a **conventional batch freeze-dryer** and the **RheaVita continuous spin freeze-dryer** using a challenging small-molecule formulation characterized by a 7-day conventional lyophilization cycle and a fill volume exceeding 50% of the vial capacity. The lyophilization cycle using continuous spin freeze-drying was conducted under two challenging spin-freezing conditions, corresponding to gas-to-vial temperature differences (ΔT) of **80 K** and **120 K**.



Figure 2. Conventional Batch Lyophilizer vs. Spin-Freeze Dryer

LYOPHILIZED PRODUCT ANALYTICAL TESTING

- **CAKE APPEARANCE By Visual Inspection**
- **RESIDUAL MOISTURE By Karl Fisher Titrator**
- **IMPURITY PROFILE By HPLC**

Results

CONVENTIONAL BATCH LYOPHILIZER	RHEA VITA SPIN-FREEZE-DRYING TECHNOLOGY

LYOPHILIZATION CYCLE PROFILE

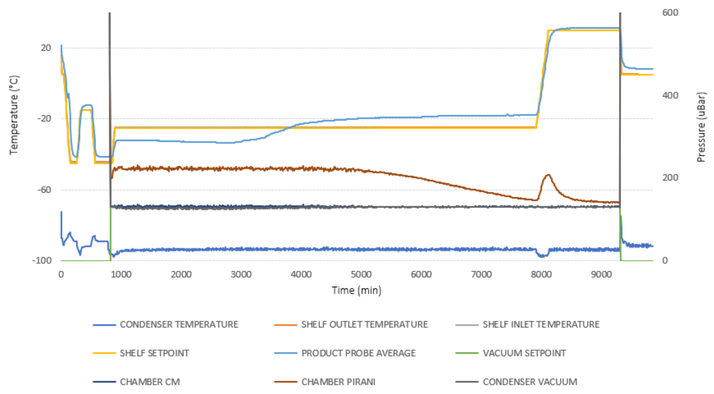


Figure 3. Lyophilization cycle profile generated with the **LyoStar III** lyophilizer for a complex small-molecule formulation (fill volume >50% of vial capacity).

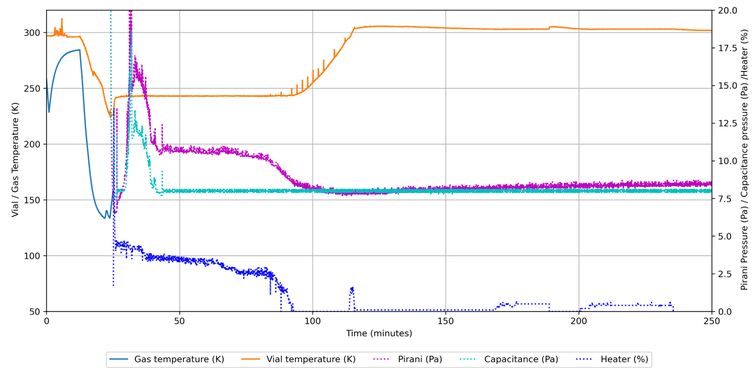


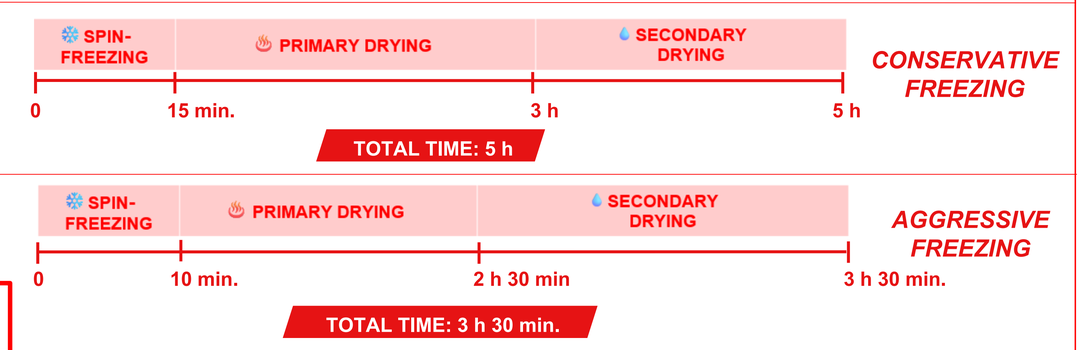
Figure 4. Lyophilization cycle profile generated with the **RheaVita** lyophilizer for a complex small-molecule formulation (fill volume >50% of vial capacity). The cycle was developed using an aggressive freezing with ΔT gas-vial of 120 K, identified as the optimal parameter, due to the longer cycle duration observed at ΔT = 80 K.

PROCESS DURATION



TOTAL TIME: 7 Days

7 Days→3 h



CRITICAL QUALITY ATTRIBUTES

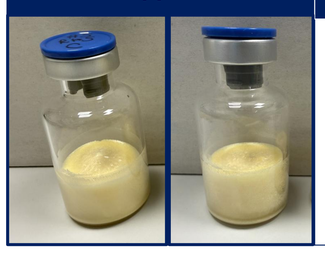
Cake Appearance	Residual Moisture %	Impurities %
	< 2	2.65

Table 1. CQAs of the lyophilized product obtained with the **LyoStar III** lyophilizer.

Cake Appearance	Residual Moisture %	Impurities %
	< 2	2.11

Table 2. CQAs of the lyophilized product obtained with the **Rhea Vita** lyophilizer, selecting the cycle with an aggressive freezing ramp.

Spin-freeze drying minimizes impurity levels by reducing process duration.

Conclusions

7 Days→ 3 h

~ 98% REDUCTION IN LYOPHILIZATION CYCLE DURATION

✓ IMPROVED CRITICAL QUALITY ATTRIBUTES

✓ SCALABLE TECHNOLOGY FOR COMPLEX FORMULATIONS

KEY MESSAGE → **Continuous Spin-Freeze -Drying Technology offers an innovative approach to dramatic accelerate the lyophilized product manufacturing while ensuring consistent product quality.**
Reducing overall cost, API needs and timelines in product development.

NOW ONGOING in the FD Laboratory →

- **Study on the application of this technology to complex formulations, including lipid nanoparticles**
- **Scale-up on the GMP production line, in collaboration with Rhea Vita**

References:
Z. Schaal et al., International Journal of Pharmaceutics 683 (2025) 126007
Lamoot et al., Biomaterials Science 11 (2023) 4327
Z. Schaal et al., European Journal of Pharmaceutical Sciences 204 (2025) 106963

Author Contact:
Emanuela Turdo, PDS Formulation Scientist
PDS Analytical & Formulation Development Lab. - Patheon Italia S.p.A (Monza site), part of Thermo Fisher Scientific
emanuela.turdo1@thermofisher.com – Mobile (+39) 331 3601536