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

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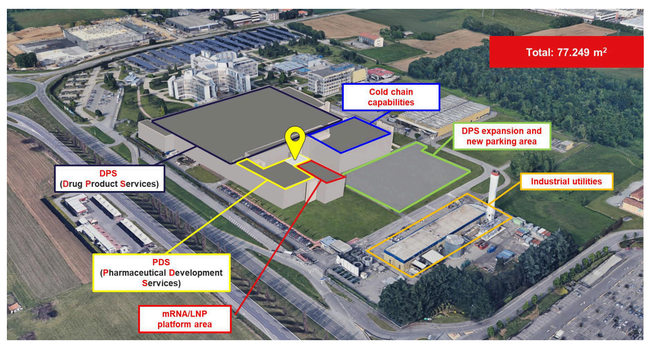


TFS Monza PDS Formulation & Analytical Development Laboratory Services and Tailor-Made Solutions

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.

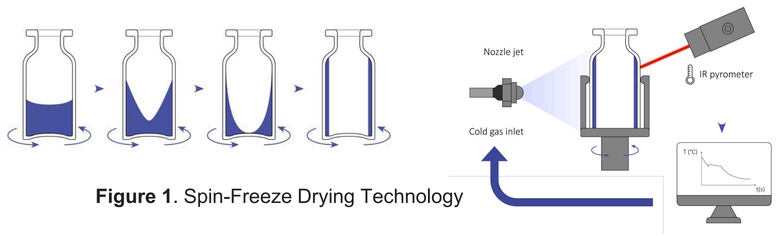


Figure 1. Spin-Freeze Drying Technology

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

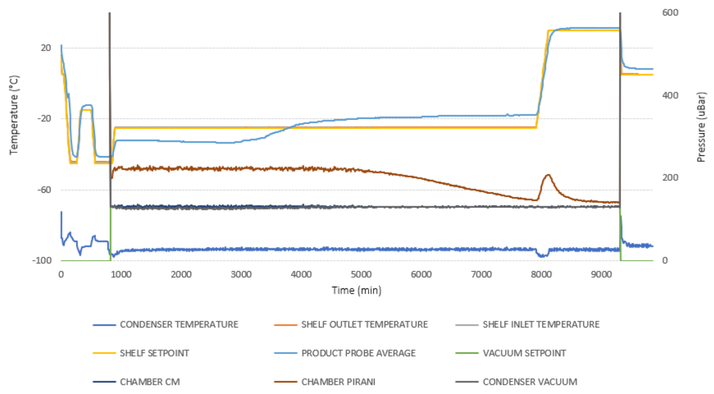


Figure 3. Lyophilization cycle profile generated with the **LyoStar III** lyophilizer for a complex small-molecule formulation (fill volume >50% of vial capacity).

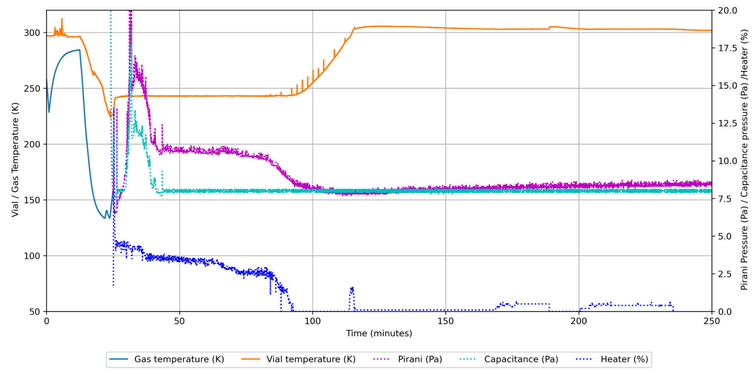
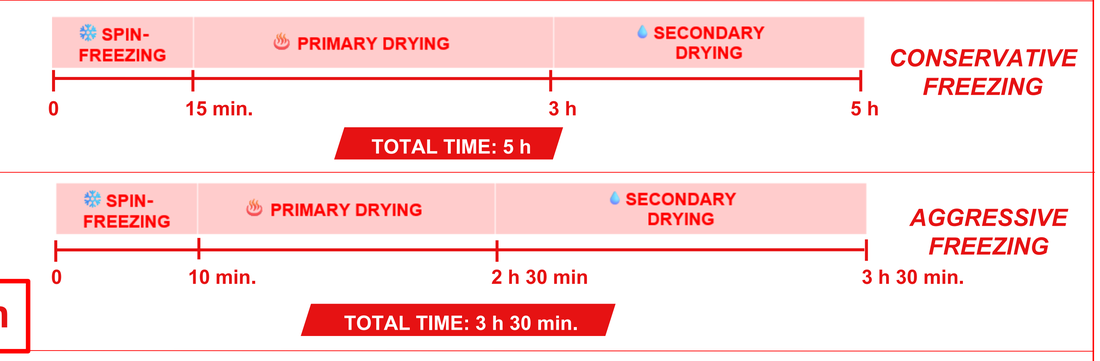


Figure 4. Lyophilization cycle profile generated with the **RheaVita** lyophilizer for a complex small-molecule formulation (fill volume >50% of vial capacity). The cycle was developed using an aggressive freezing with ΔT gas-vial of 120 K, identified as the optimal parameter, due to the longer cycle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

PROCESS DURATION

TOTAL TIME: 7 Days

7 Days→3 h



CRITICAL QUALITY ATTRIBUTES

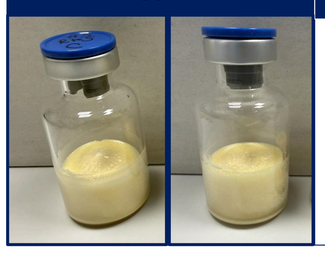
Cake Appearance	Residual Moisture %	Impurities %
	< 2	2.65

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

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