

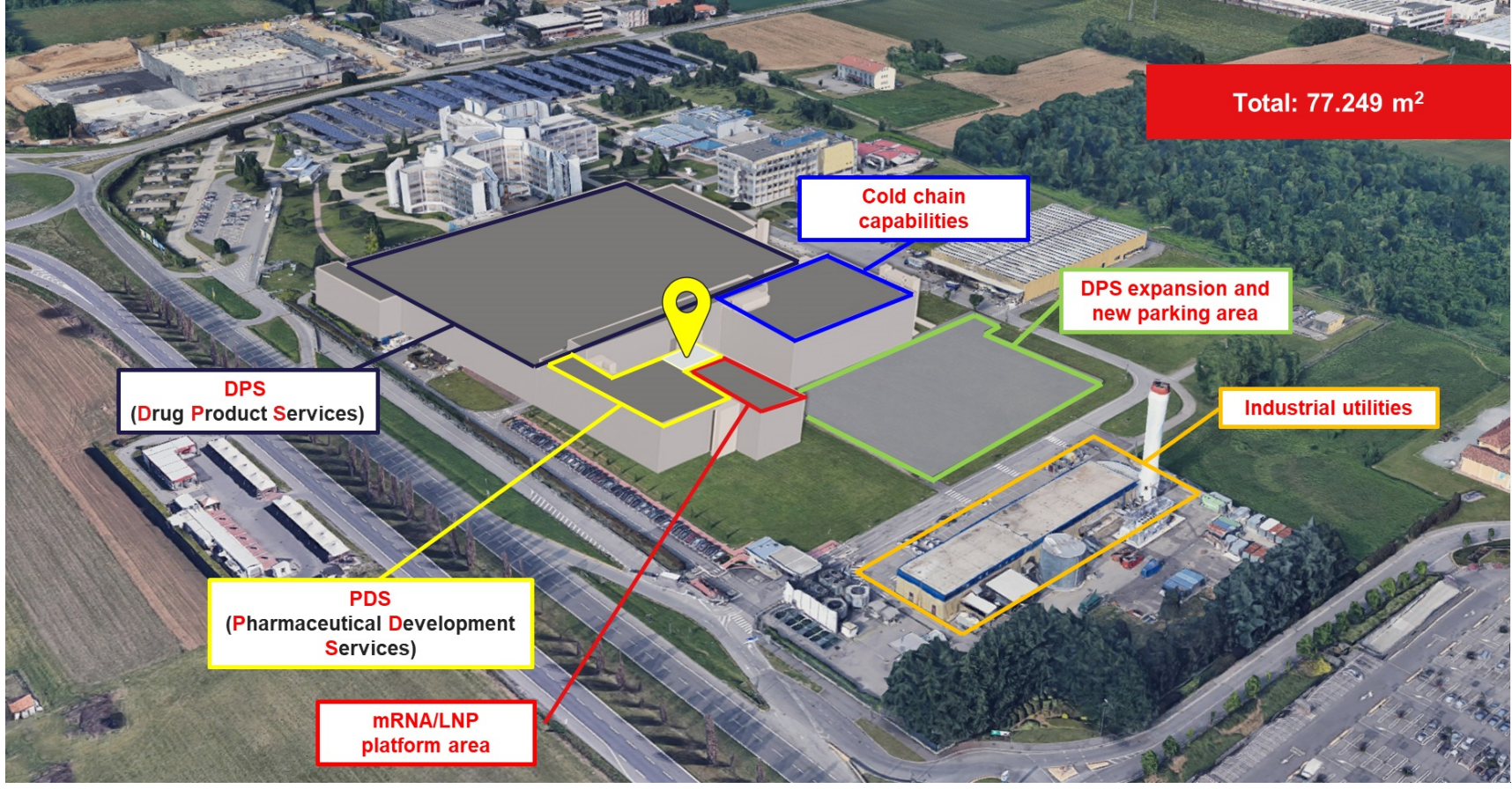
From Conventional Batch Lyophilizer to Continuous Spin-Freeze-Drying Technology: Lyophilized Drug Product in hours instead of days

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TFS Monza Campus



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

Early Stage

- Pre-formulation Studies & Prototype
- Familiarization Study & Compounding Design
- Purification/Filtration Design
- Lyophilization Cycle Development & Scale-up
- Fill Volume Determination
- Spiking Study (oxidant)
- Terminal Sterilization Study
- Toxicological Batch Manufacturing

Middle Stage

- Product Contact Part Compatibility & In-Use Studies
- Lyophilization Cycle Robustness (DoE)
- Formulation Robustness (DoE)
- Holding Time Studies
- Freeze-thaw Studies
- Pumping Recirculation Studies
- Mixing Study
- 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.

Methods

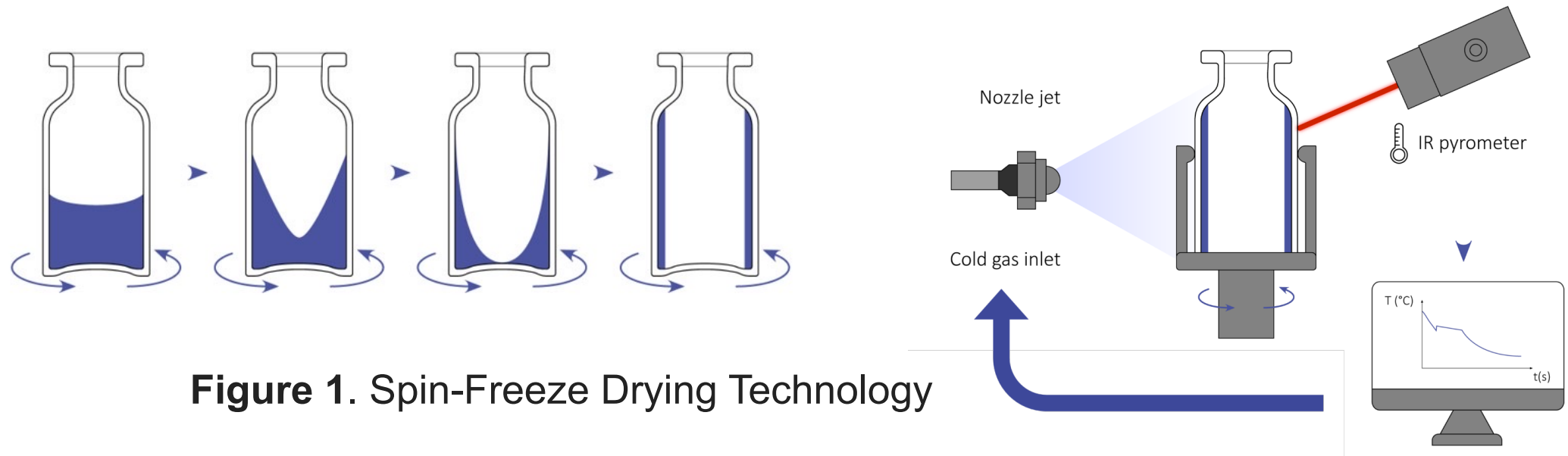


Figure 1. Spin-Freeze Drying Technology

OBJECTIVES OF THE STUDY

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

Results

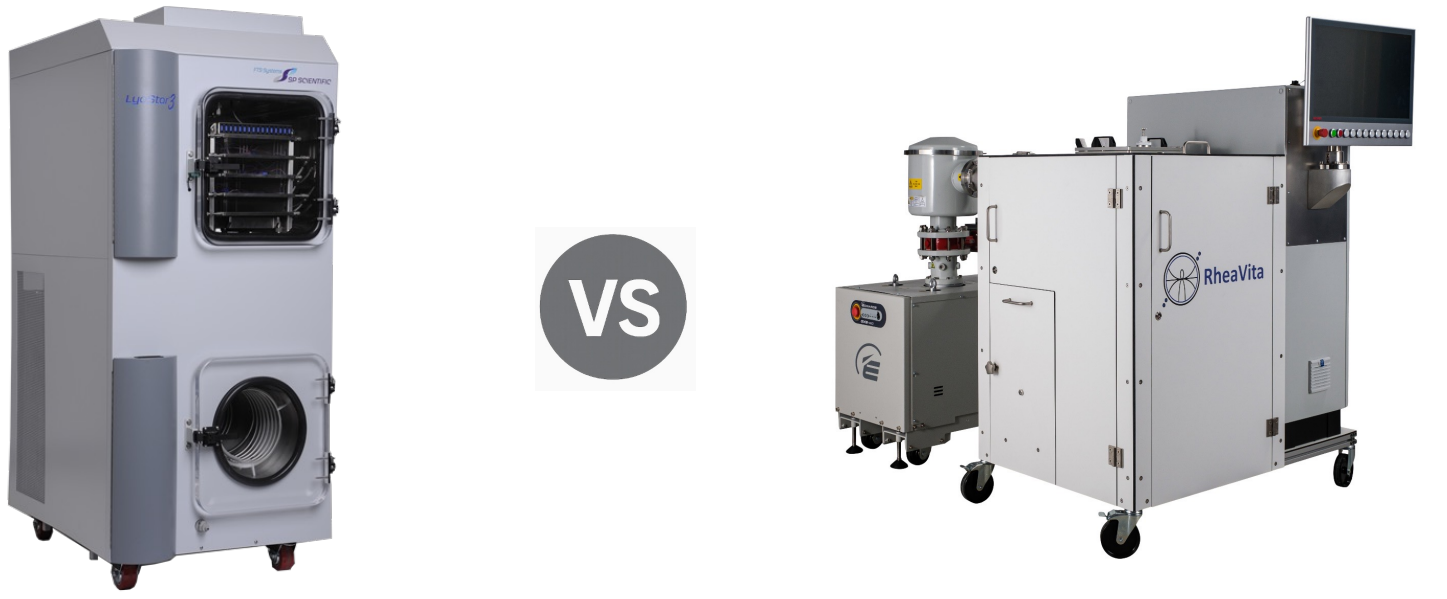


Figure 2. Conventional Batch Lyophilizer vs. Spin-Freeze Dryer

LYOPHILIZED PRODUCT ANALYTICAL TESTING

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

CONVENTIONAL BATCH LYOPHILIZER

RHEA VITA SPIN-FREEZE-DRYING TECHNOLOGY

LYOPHILIZATION CYCLE PROFILE

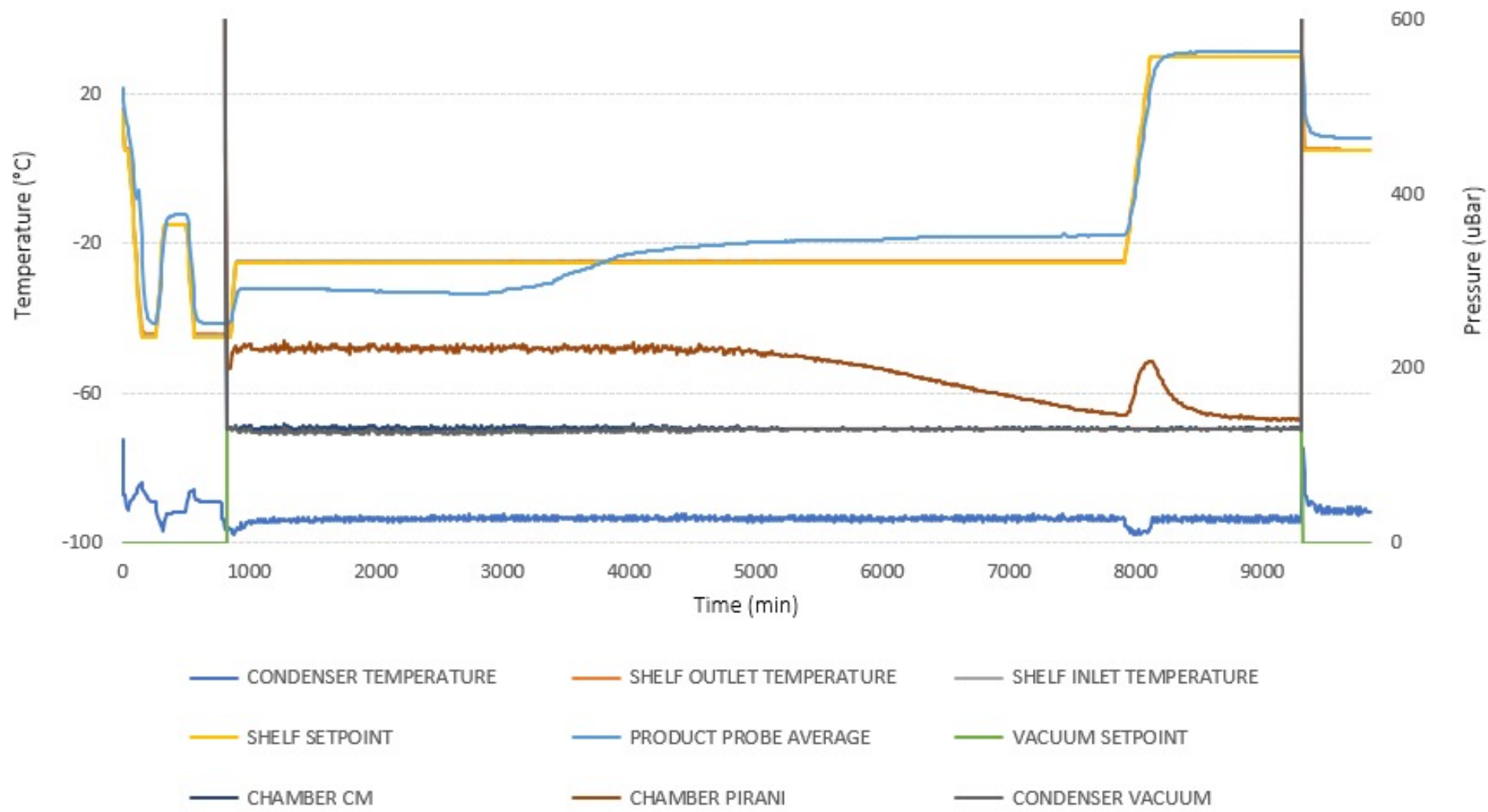


Figure 3. Lyophilization cycle profile generated with the LyoStar III lyophilizer for a complex small-molecule formulation (fill volume >50% of vial capacity).

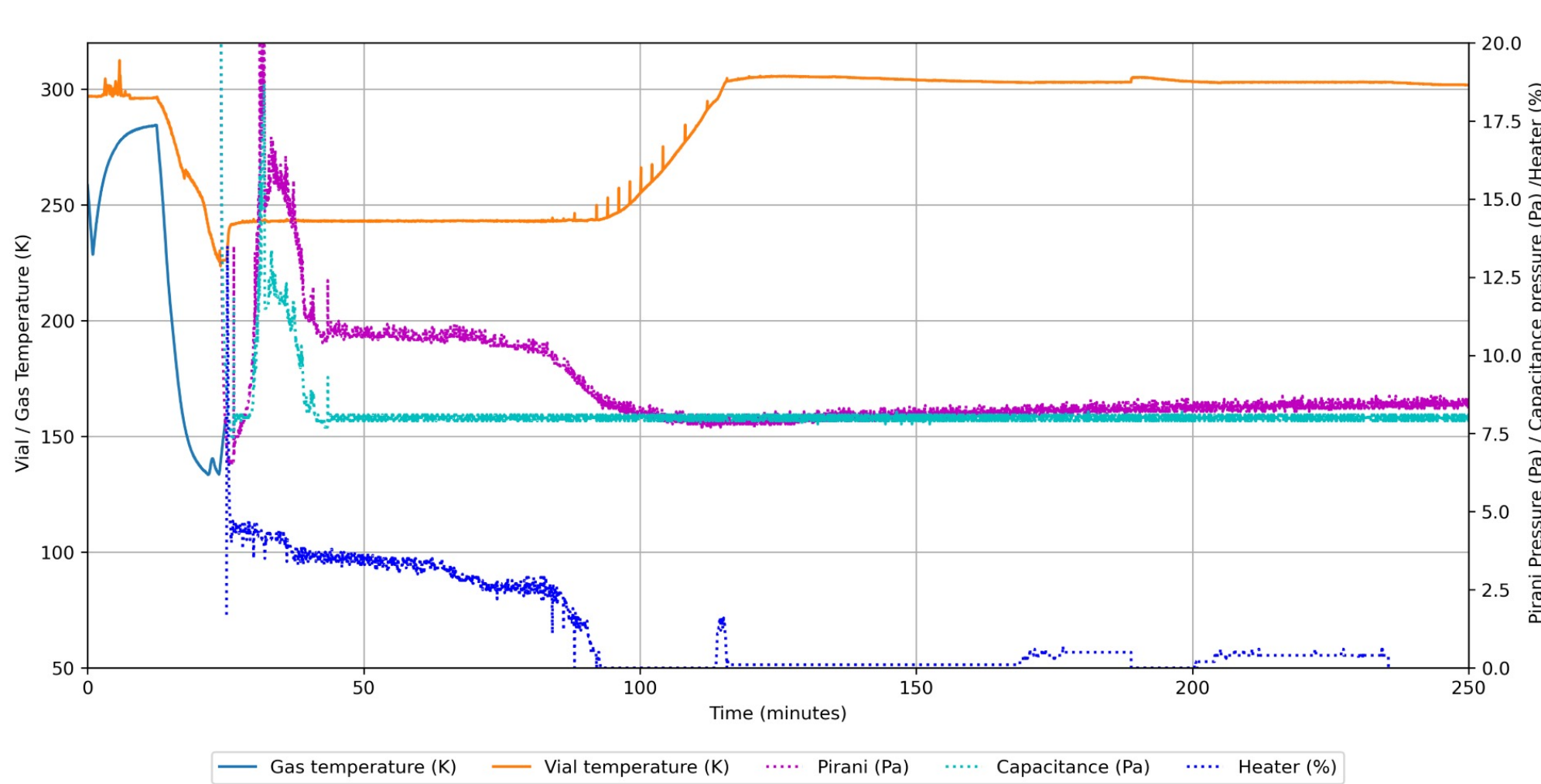
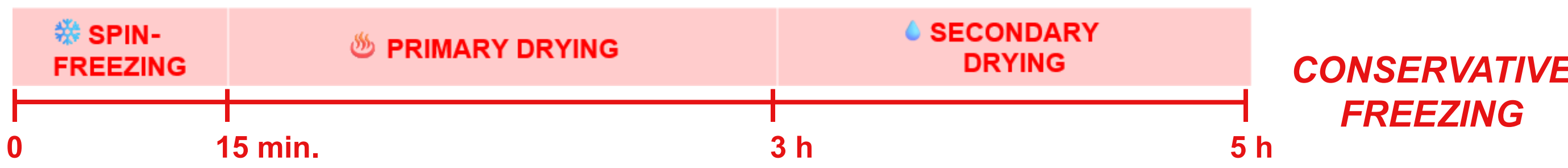


Figure 4. Lyophilization cycle profile generated with the RheaVita lyophilizer for a complex small-molecule formulation (fill volume >50% of vial capacity). The cycle was developed using an aggressive freezing with ΔT gas-vial of 120 K, identified as the optimal parameter, due to the longer cycle duration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

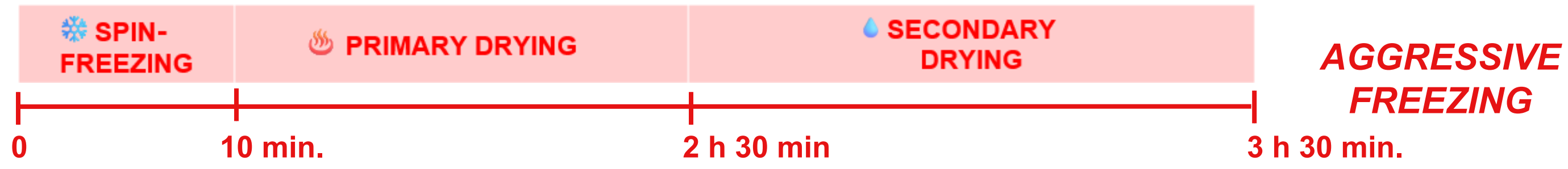
PROCESS DURATION



TOTAL TIME: 7 Days



TOTAL TIME: 5 h



TOTAL TIME: 3 h 30 min.

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