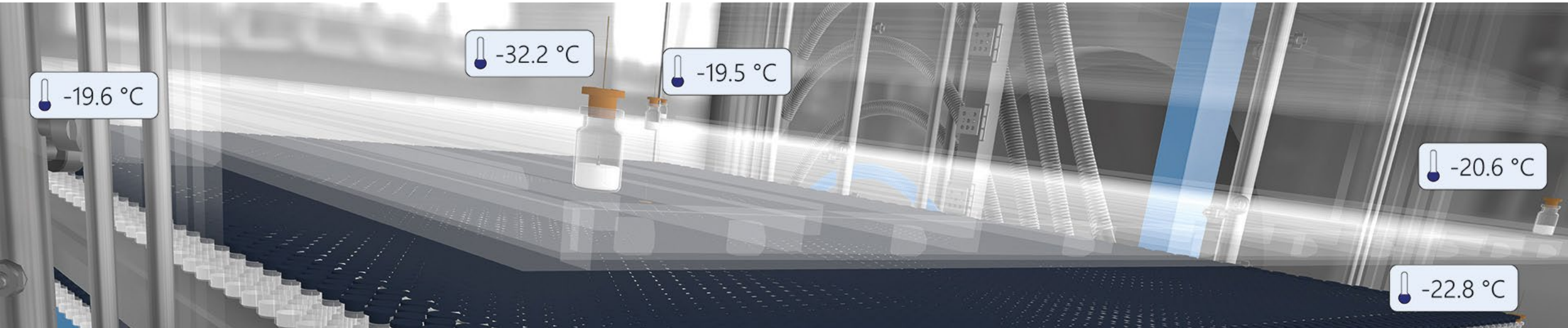
From Product Temperature to Best Process Performance

Can a standardized transfer method make freeze-drying more efficient?

Can real-world Tp data become the evidence base for the next run, tech transfer, PPQ, and CMC?

Anton Mangold - Founder and CEO - Tempris GmbH



Agenda

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What are we talking about:

- The Biggest Pain Points in Lyophilization
- Freeze-drying **principles and the importance of Tp**
- Tempris Technology and Process Integration Options
- Case Study
- How **LyoCLC accelerates** process parameter estimation
- Best Process performance: Lyo Cycle simulation
- Commercial impact: why this saves you time and money
- **FDA Advanced Manufacturing Technology Designation**
- Q&A and personal exchange at our tabletop

The Biggest Pain Points in Lyophilization

From Process Development to Regulatory Approval

Early uncertainty leads to later rework, delays, costs, and CMC risk.

1. Formulation & Feasibility
2. Process development
3. Analytical methods
4. Scale-up & Transfer
5. PPQ / Validation
6. CMC / Submission
7. Review & Approval

Where the problems arise

Stage 1–2
Tg', Tc, formulation limits, early cycle assumptions

Stage 4–5
Scale-up, engineering runs, PPQ readiness, rework risk

Stage 6–7
CMC data gaps, inquiries, and review delays

Indicative Timeline Impact

+15–34 months

due to rework, delayed decisions, and regulatory inquiries

Indicative Cost Impact

€ 5-30 M+

depending on product, organization, equipment, and regulatory region

(1) Life-saving medications reach patients too late

(2) Production capacity loss

20-30%

(3) Loss of Effective Patent Life:

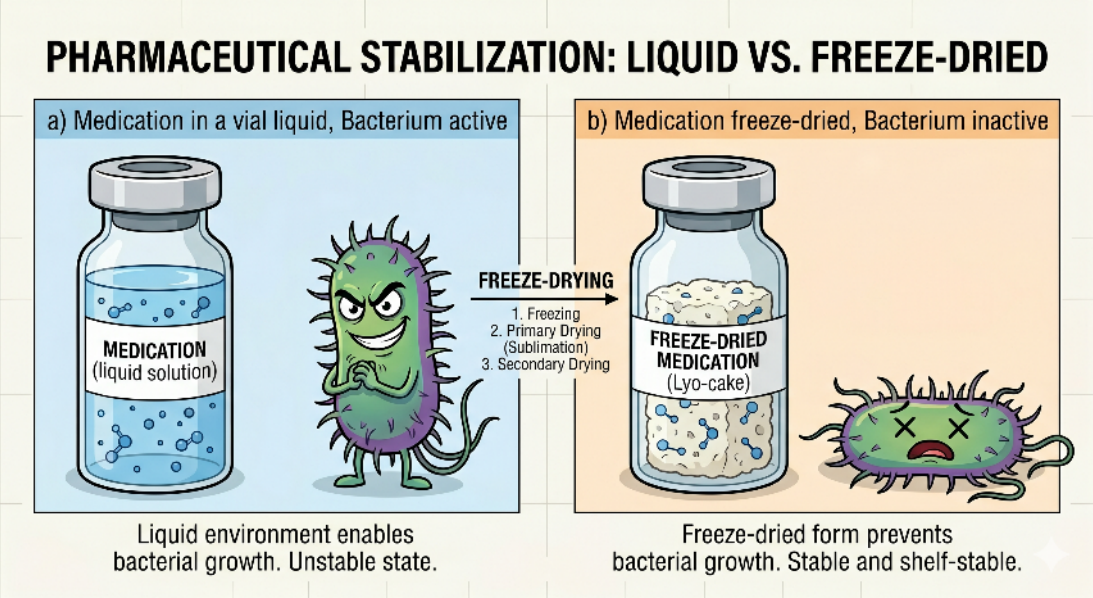
1-2 years

The transfer method does not begin with tech transfer.
It begins where assumptions about early product state are made.

Why freeze-drying?

Many classical small-molecule drug classes are mature and largely genericized, while future value creation is increasingly shifting toward complex, biology-driven therapies with high structural and functional diversity.

The future lies in complex, biology-driven therapies — and their sensitivity to degradation, aggregation, and liquid-state instability makes lyophilization a strategic enabler for sterile, stable, and scalable drug products.



The water should be removed without damaging the active ingredient. Freeze-drying provides this stabilization.

The temperature and pressure trick

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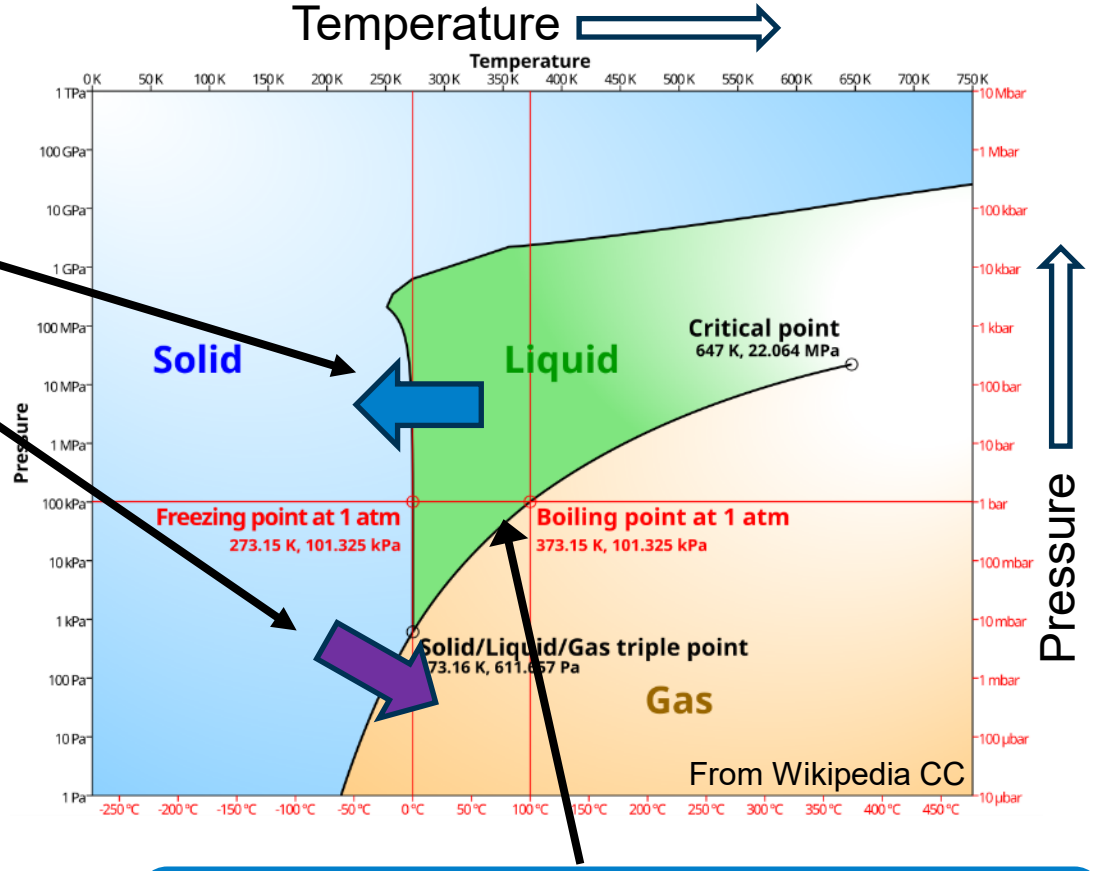
Freeze-drying as a minor detour:

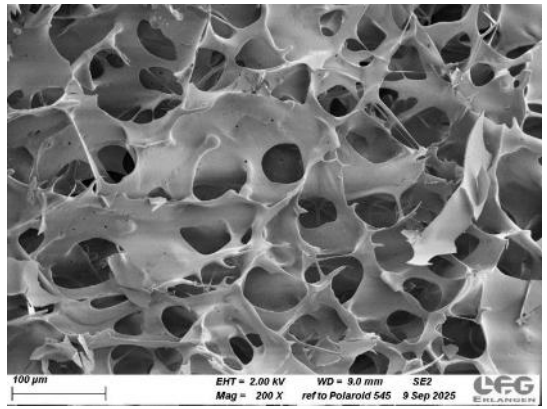
- freeze, liquid to solid ice,
- dry by direct transition from solid to gas.

This <u>does not</u> require <u>high temperatures</u>, and the active ingredient is not damaged.

Phase diagram of water:

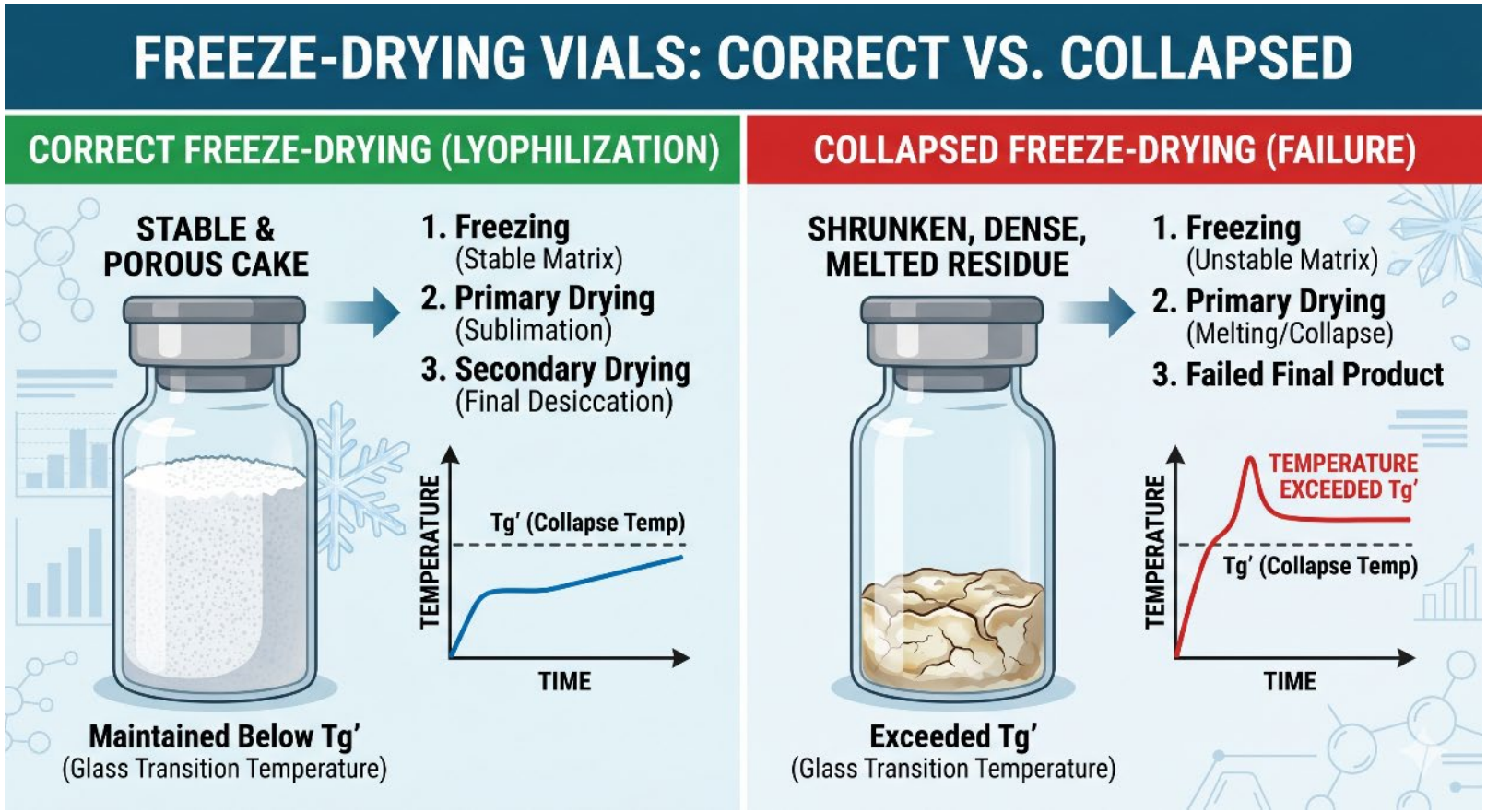


The resulting product has a sponge-like structure and is highly water-soluble. Important for the correct dosage during use!



The kitchen solution is heat: a preserving jar for jam. However, sensible pharmaceutical products cannot survive that.

Product Temperature is most important

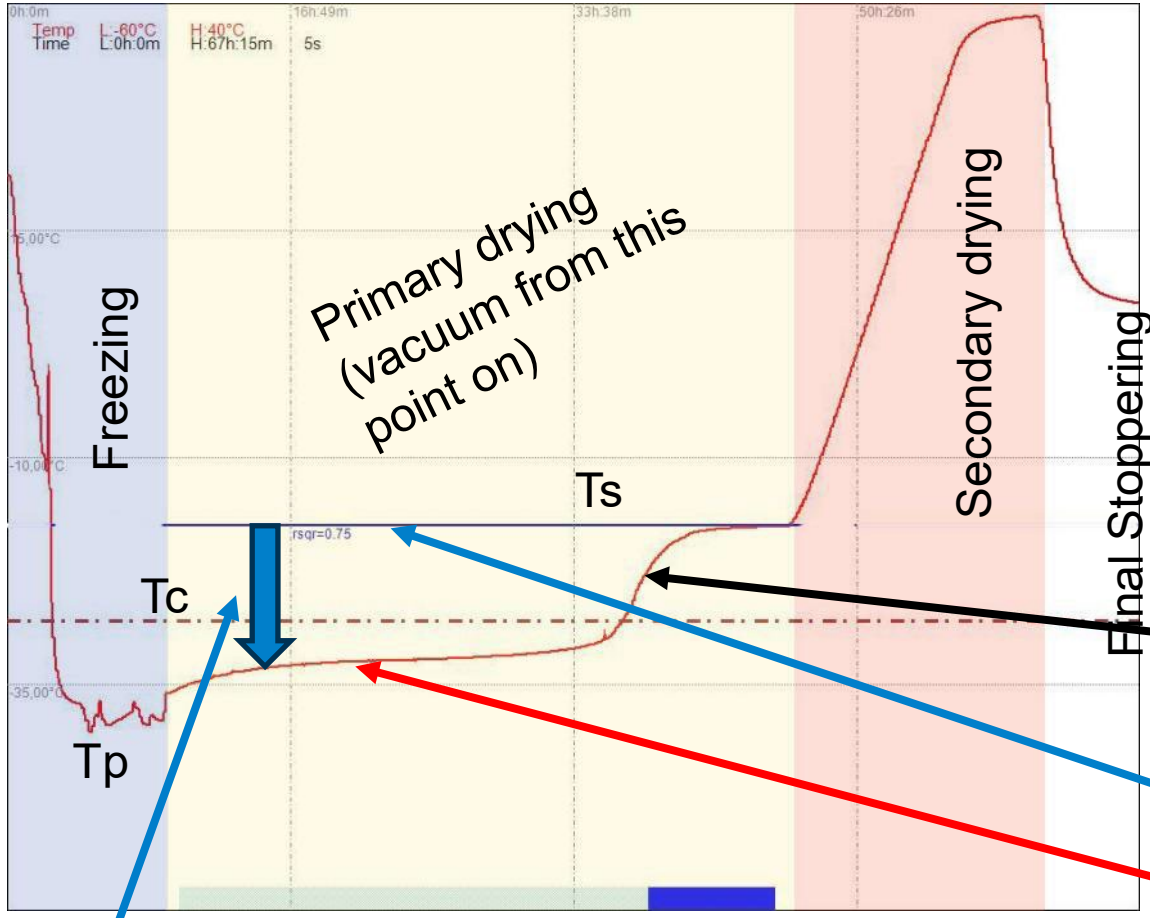


Once the collapse temperature, which is very near to the glass transition Temperature Tg, is exceeded, the sublimation surface closes and sublimation will no longer properly occur. The sponge (glass) structure converts to some “rubbery” structure which finally causes a collapse of the cake.

This is why the product temperature Tp is the most important dynamic parameter. It directly documents the quality!

Lyo-Process Steps

Product temperature measurement (Tempris):



Sublimation removes heat from the product. This heat must be supplied by the heated shelf-surface, and an equilibrium is established.

This continues until the ice has sublimated. Afterward, the product takes the shelf temperature.

If Tg' (Tc) is exceeded too early, the product will be damaged. If Tp is too low, it becomes uneconomical.

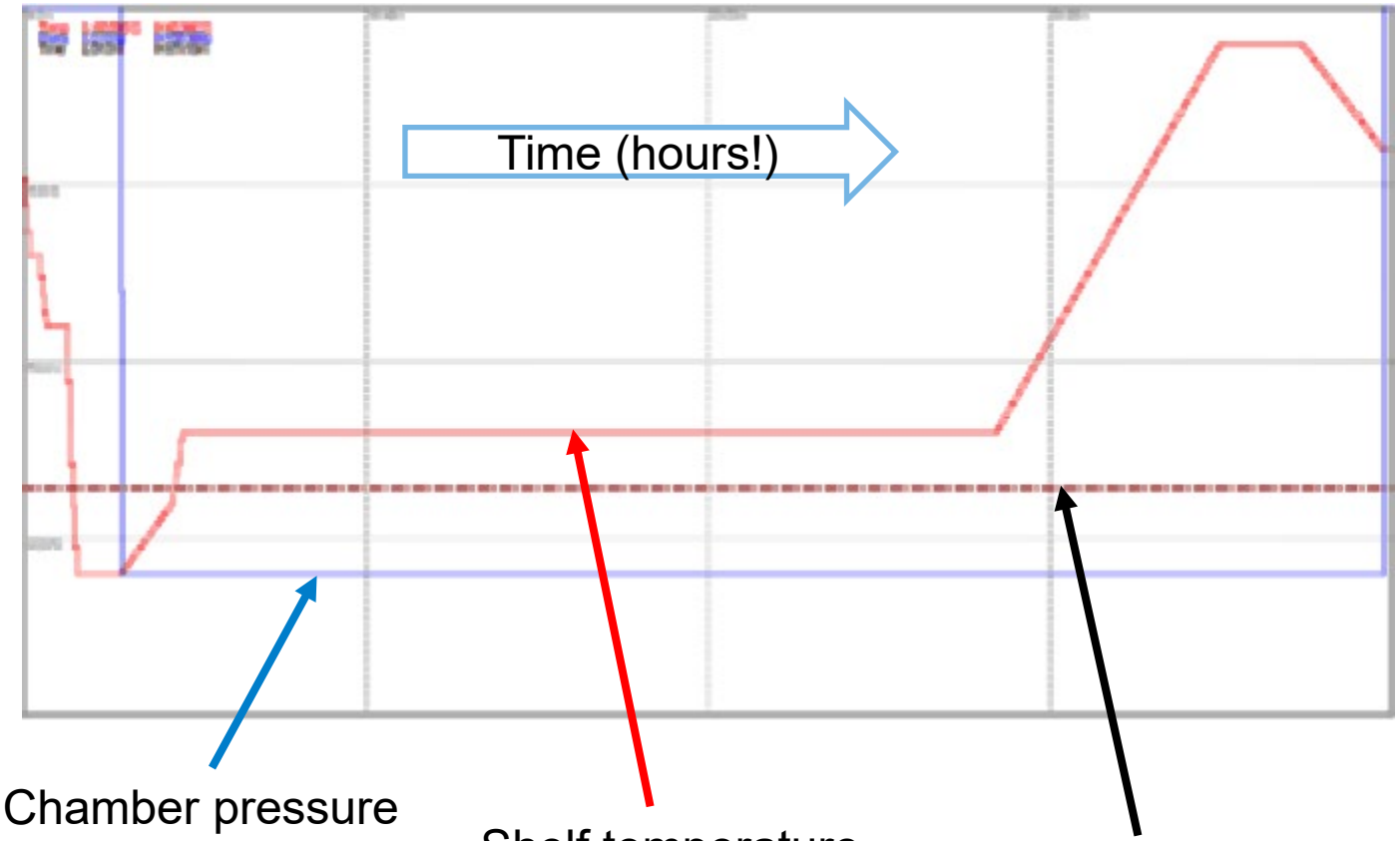
Critical transition: Ice largely sublimated. Flat ice front becomes cone-shaped (too small to collapse if processed correctly)

Determined vial specific shelf temperature Ts (Tempris)

Measured product temperature Tp (Tempris)

Decrease in Tp due to sublimation (energy requirement; enthalpy)

Lyo-Process Steps



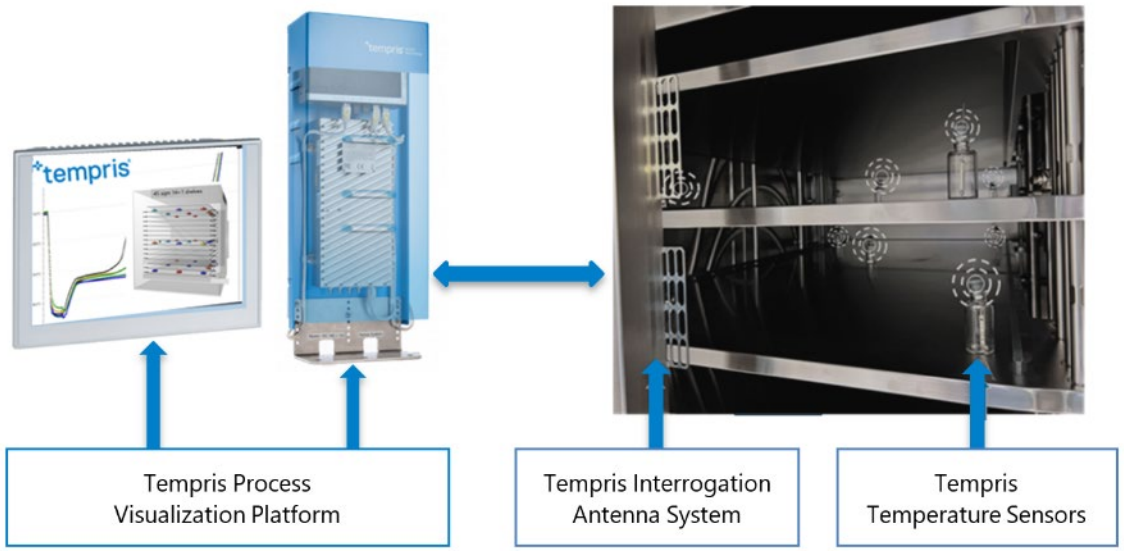
The need to measure process parameters is obvious. In any case:

- Chamber pressure: Unproblematic; capacitive pressure gauge, Pirani gauge for vapor flow, TDLAS etc.
- Shelf surface temperature: *In principle* known as set by/to the freeze dryer controller (fluid inside shelf plates)
- Product temperature: **The crux of the matter!**

Tempris System Solution

Tempris measures Tp inside the vial - in real-time

No cables. No batteries. No product interference.



Integrated system for freeze-drying:

- Sensors measure real product temperature (Tp) inside the vial
- RF technology transmits data wirelessly
- TLM processes and visualizes data in real time
- Fully integrated into SCADA / HMI / Virtual Machine
- Ready for automated sensor placement using robotics

Tempris:

✓ Wireless
✓ Battery-free
✓ Fully integrated in process

✓ Sterile and integrable
✓ Annex 1 compliant
✓ Validated for clinical use

Tempris System Solution

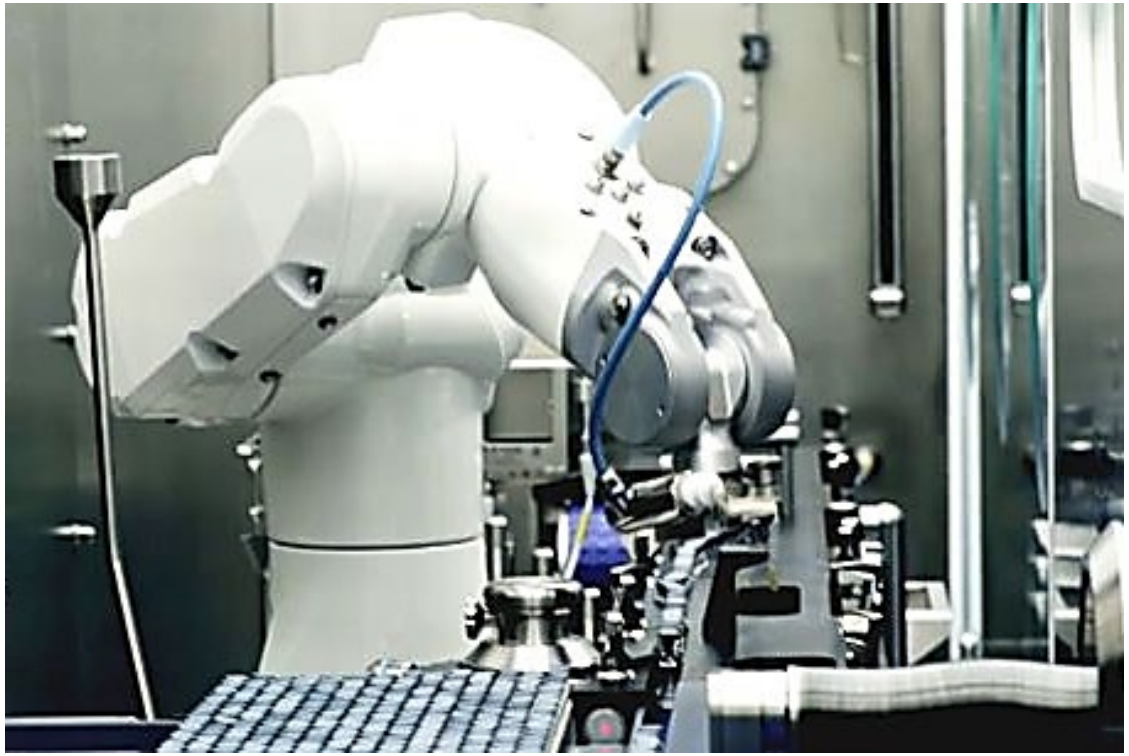
Product-level PAT and LyoCLC intelligence for GMP lyophilization

Tempris provides vial-level product temperature measurement and the LyoCLC layer to support PPQ and CPV.

Interface coordination with your supplier partners for product-level process control.

From assumptions to a traceable product evidence — reducing rework, safety margins, and CMC risk.

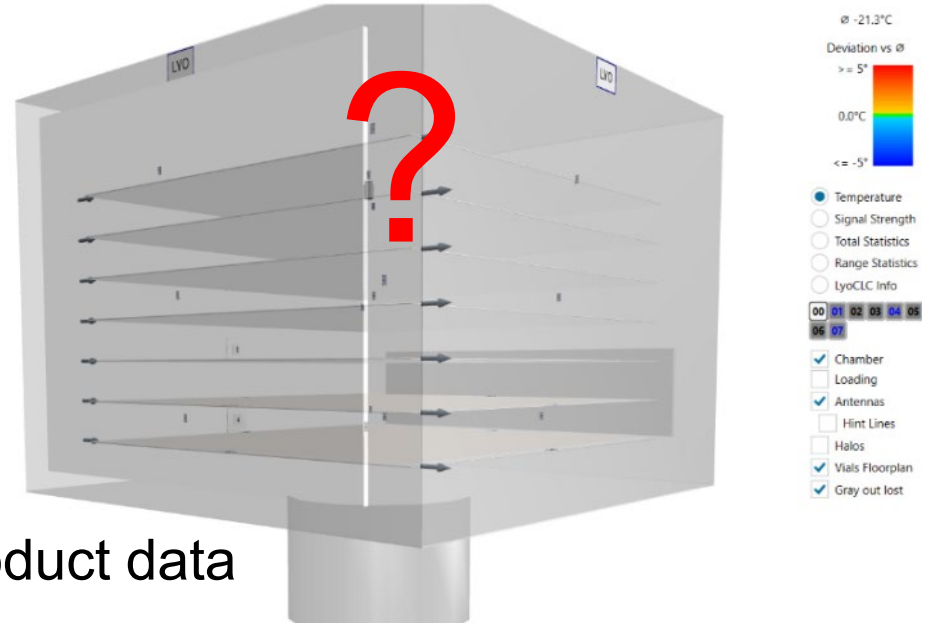
Precisely centered, identified sensors for vial-level traceability.



Annex 1-compliant robotic sensor insertion with full vial-level traceability.

Case Study

Legacy processes work - but we do not fully understand them



Processes are permitted and stable however:

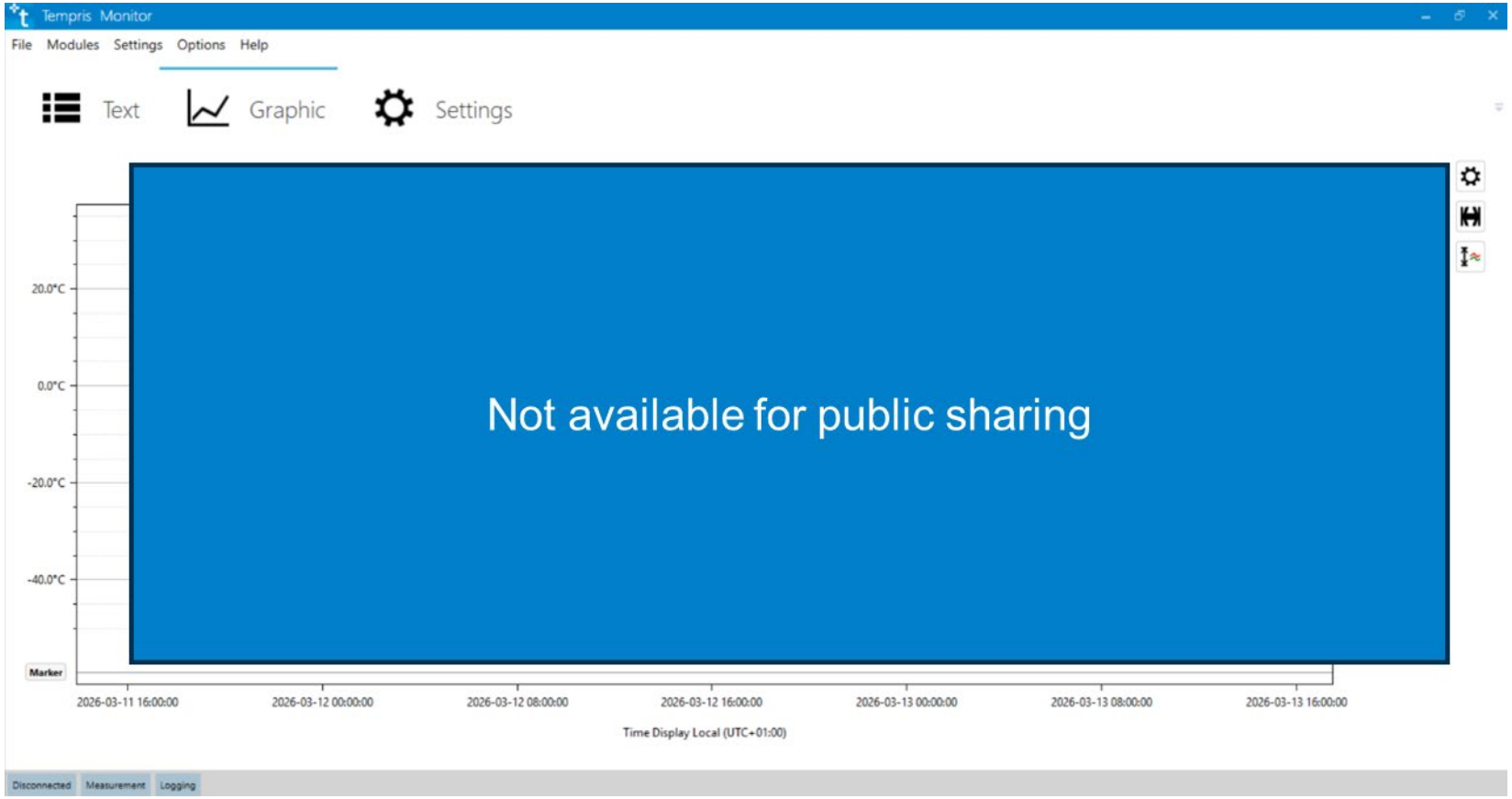
- missing development data
- unknown product temperature
- conservative safety margins

Decisions are based on experience, not on product data

Data quality and comparability

Clear measurement points on critical positions at the shelves

- Systematic mapping of product temperature distribution
- Comparability across scales and devices
- Data transfer and scaling



Case Study

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Why Current Approach No Longer Works:

Traditional product temperature measurement does not provide reliable, comparable data for process understanding and scale-up.

HOW IT IS DONE TODAY

Traditional Approach

- Sensors are placed manually
- Sensor position varies between batches
- No control over exact measurement location
- Limited reproducibility

WHAT THIS CAUSES

What this leads to:

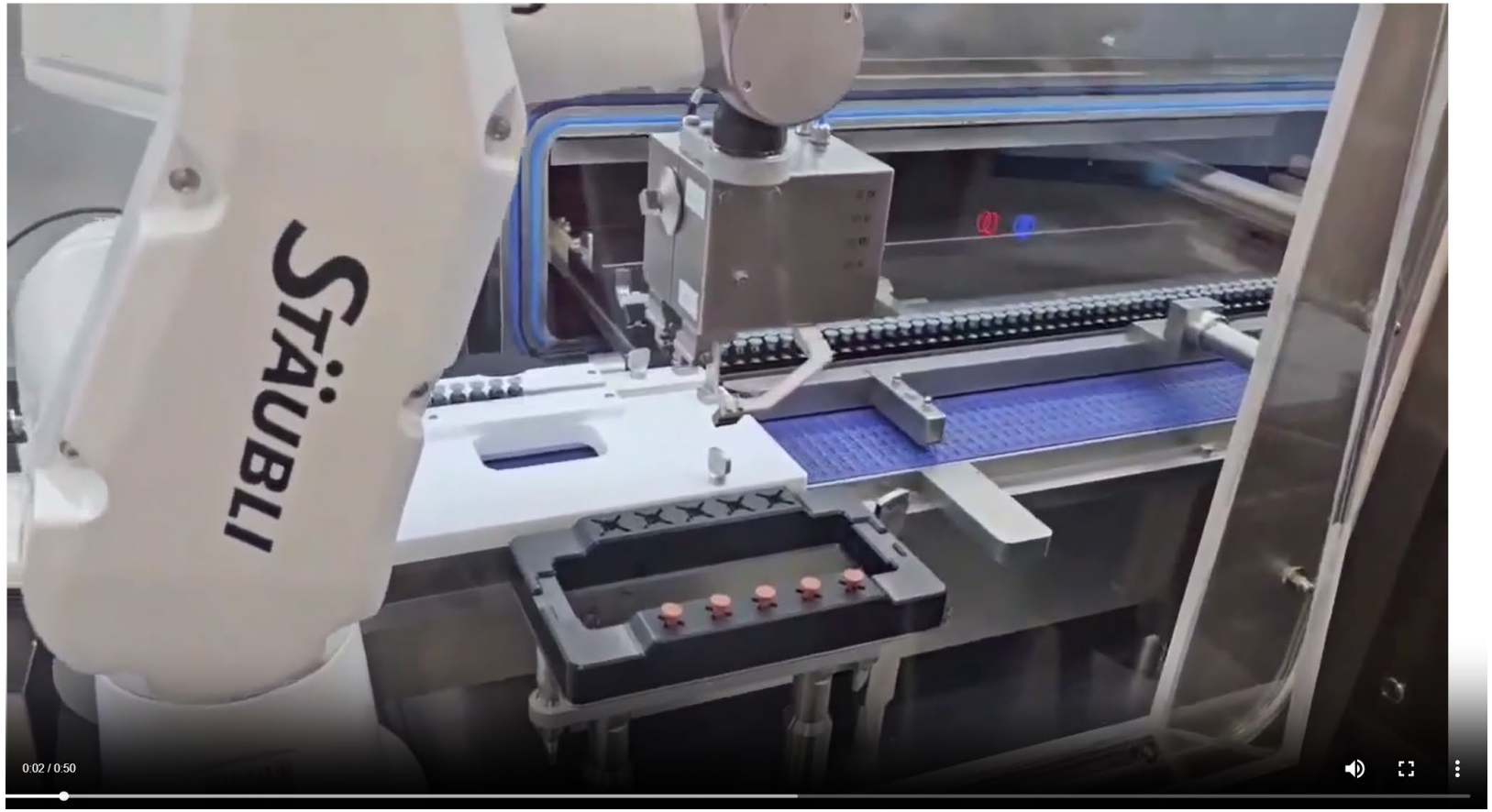
- Each batch is measured differently
- Data is not comparable across runs and equipment
- No certainty that the same locations are monitored
- Process understanding remains incomplete

Critical Impact in Scale-Up and New Facilities

- We cannot reliably compare processes
- We cannot identify consistent hot and cold spots
- We cannot build the process on robust data

Traditional temperature measurement is no longer sufficient as an engineering tool

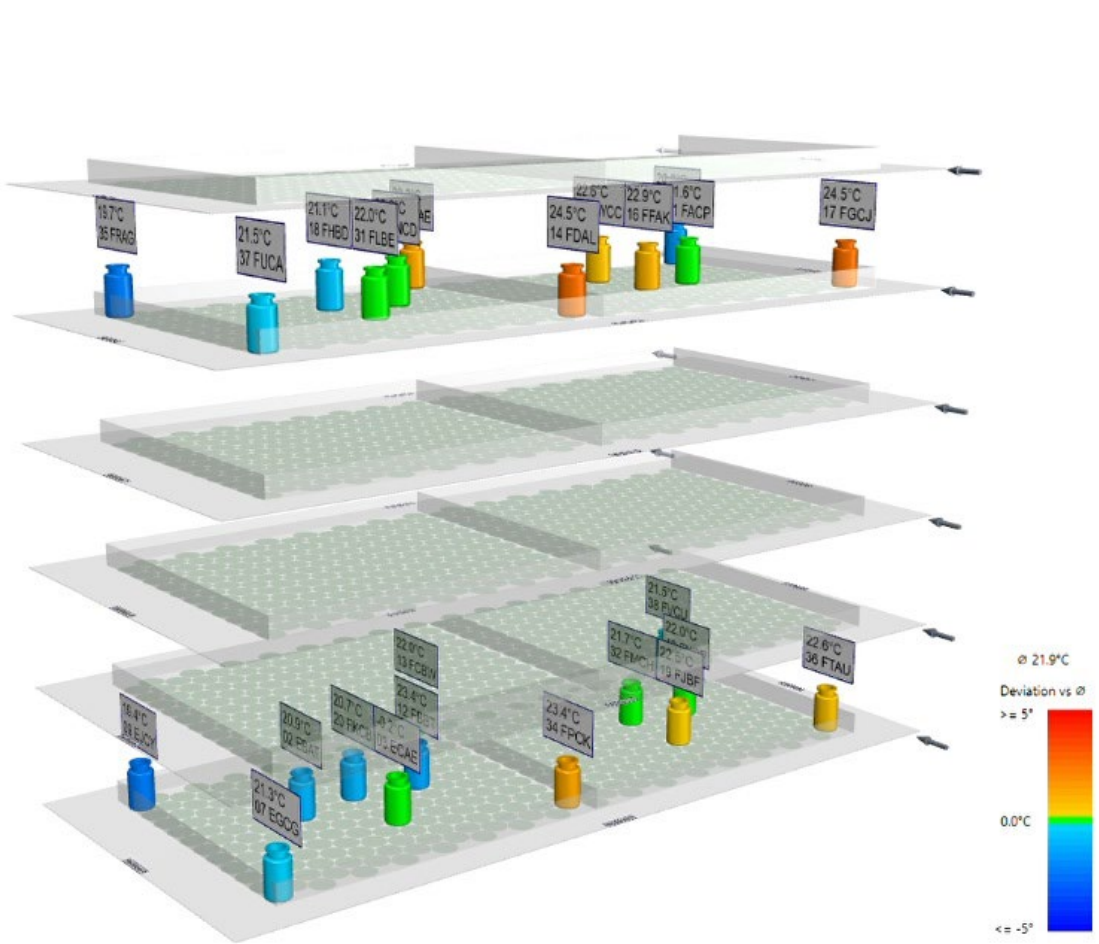
Case Study



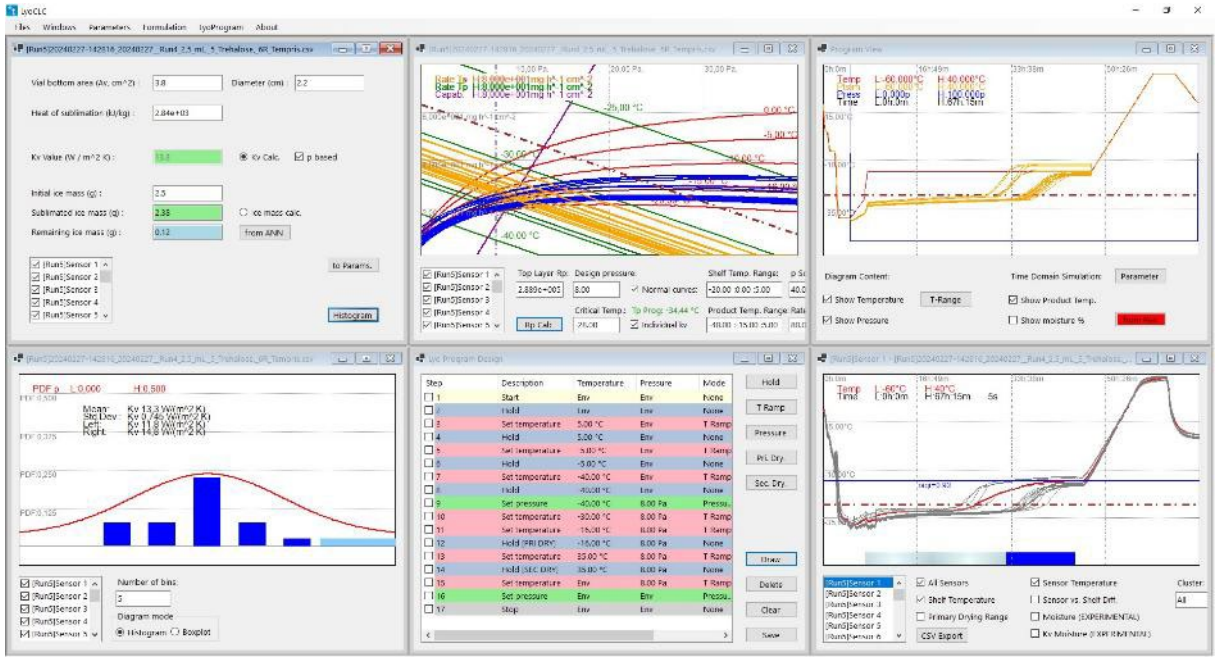
https://www.tempris.com/tempris-video/Tempris-Sensor-Loading-with-Robotic-System.html

Several robot solutions have been implemented in collaboration with
Hof, Optima, Dara, etc.

Digitalization for Process Analytics

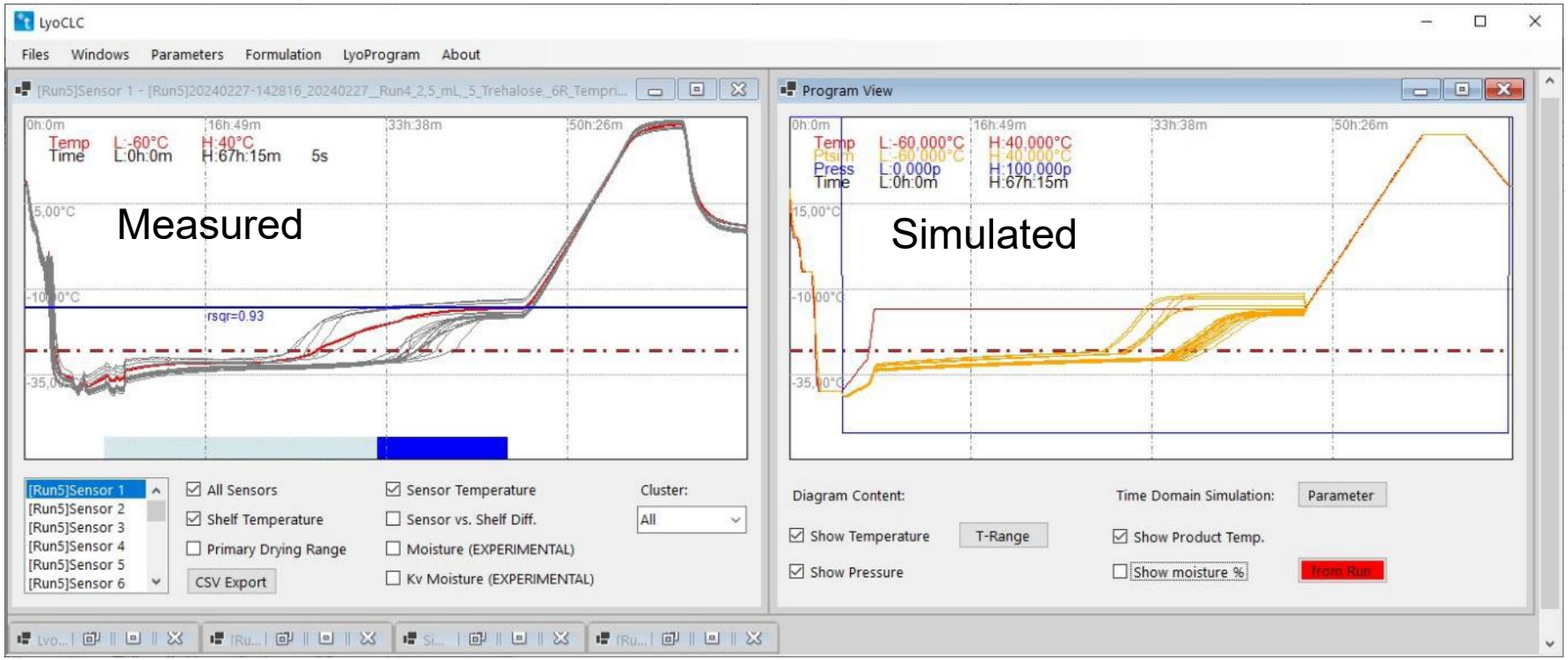


Digital Twin with Hot & Cold Spot Monitoring



Tempris is a complete software solution with an integrated database and a wide range of analysis options **with automation interfaces** to the FD Control System, including the digital twin.

Lyo Cycle & Simulation



- After processing several runs, the parameters are automatically extracted.
- These parameters are incorporated into a simulation, whose accuracy can be immediately verified visually.
- The next freeze-drying run is first simulated using the recorded data from Run 1 for Run 2. In this process, all previous parameters are mapped within the design space. To optimize the process, the new target values are calculated manually or automatically using LyoCLC. The new parameters (settings) are displayed in the simulation window as a recipe suggestion.
- This saves costs and ensures quality.

Measure → Extract parameters → Simulate → Optimized production

How Tempris LyoCLC Turns Lyo Pain Points into GMP Transfer Confidence

From real product temperature to standardized process understanding, transfer evidence, and GMP-relevant decision

Root cause: Early product uncertainty creates late-stage rework, PPQ delays, CMC questions, and hidden capacity losses.

LyoCLC answer: Real vial-level product temperature is converted into product-process evidence for development, transfer, PPQ, and CPV.

LyoCLC decision chain

1 Measure real Tp
Tempris sensors + Digital Twin

→

2 Interpret in LyoCLC
Kv/Rp, endpoint, margins

→

3 Build GMP evidence
Scale-up, PPQ, CPV

→

4 Decide with confidence
Transfer, capacity, CMC

Where problems arise — and how Tempris LyoCLC addresses them

Stage 1–2 Product & Cycle Definition

Pain: Tg′/Tc limits known, but real vial behavior is assumed.

LyoCLC: Tp profiles, critical-temperature margins, early drying insight.

Result: Safer cycle definition and fewer iterations.

Stage 3–5 Scale-up & PPQ Readiness

Pain: Equipment differences, hot/cold spots, unclear transfer comparability.

LyoCLC: Digital Twin mapping, standardized sensor positions, Kv/Rp and residual-moisture correlation.

Result: Faster transfer readiness and stronger PPQ rationale.

Stage 6–7 CMC / Review / CPV

Pain: Data gaps, review questions, limited lifecycle visibility.

LyoCLC: Product-temperature evidence package, robustness documentation, CPV trends.

Result: Stronger CMC confidence and reduced lifecycle risk.

Business impact

Reduced timeline risk
Fewer late-stage rework loops

Reduced cost exposure
Fewer unnecessary engineering runs

Potential capacity gain
Data-based safety-margin reduction

Protected product value
Earlier readiness supports patient supply and launch value

LyoCLC does not simply collect more data — it converts real product temperature into a GMP-relevant decision platform for faster, safer, and more confident lyophilization decisions.

Thank You

A sincere thank you to all pharmaceutical companies, equipment suppliers, automation partners, and scientific experts who have supported Tempris on this journey.
Together, we are helping lyophilization move from process assumptions to traceable product evidence — creating the foundation for better transfer, PPQ readiness, CPV, and Pharma 4.0.

Ready to turn product temperature into process performance?
Let's discuss your path forward.

Contact

For more details, please contact us

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