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# Tempris GmbH

## Transforming Lyophilization with Innovative Temperature Monitoring

**L** yophilization, or freeze-drying, is vital in the bio/pharmaceutical industry for drugs with unstable ingredients or requiring an extended shelf life. Among the various phases of lyophilization, precise temperature control during primary drying is paramount to ensuring product integrity.

Traditionally, wired thermocouples or resistance thermal detectors (RTDs) were used to measure the temperature in the API manufacturing process. However, manual insertion of sensors posed an increased risk of contamination to patients, prompting the reinforcement of safety regulations. In response to stringent regulatory requirements under Good Manufacturing Practice (GMP), pharmaceutical companies are increasingly turning to Process Analytical Technologies (PAT initiatives). Previously, the lack of technology for real-time product temperature measurement during the lyophilization process meant that pharmaceutical companies had to rely on multivariate data to simulate process parameters for each Active Pharmaceutical Ingredient (API) filled in containers and freeze-drying system size. Unfortunately, this data only approximate real-time measurement, which means that significant safety margins have to be used. There is a risk that the safety margins may not cover all critical quality attributes (CQA) within the design space, potentially allowing for errors.

Approval of a product based on these unreliable parameters may lead to time and cost disadvantages throughout the entire product life cycle.

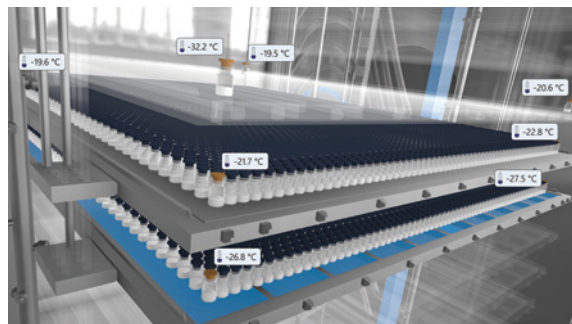
Optimization of such processes is crucial to scaling up, as it can lead to time and cost savings of up to 20 percent.

Therefore, the pharmaceutical industry is actively seeking innovative solutions to enhance temperature monitoring during lyophilization, ensuring adherence to GMP regulations and improving the reliability of critical quality attribute measurements.

To overcome these challenges, Tempris has successfully developed a state-of-the-art temperature monitoring technology solution. The device can accurately determine the temperature of products within various types of containers, regardless of their position in the lyophilizer load. It can effectively monitor



temperatures even when the loading process is done either manually or automatically. This technology provides real-time data, facilitating effective process control. Tempris provides customers with innovative equipment and designs, along with consultancy services on effectively implementing these advancements in regulatory submissions.



### A Game-Changing Solution Emerges

Tempris offers an innovative wireless, battery-free temperature sensor providing real-time measurements. The wireless feature is paramount, particularly in modern lyophilizers equipped with automated loading systems, eliminating the feasibility of the traditional thermocouple method that relies on manual placement. The

battery-free design is equally crucial, as conventional battery-based systems pose a contamination risk to GMP sterile products and also introduce heat during the measurement process, potentially causing errors in the recorded measurements. With Tempris' technology and the appropriate antenna setup, the probes can obtain product temperature readings anywhere within the equipment or load and help to overcome the uniformity issues plaguing the lyophilization process for years.

As trailblazers in the field, Tempris collaborated with a partner to create an automated robot solution, ensuring comprehensive traceability by consistently placing sensors in critical positions. This facilitates batch-to-batch comparability across different freeze dryers. Tempris has tailored its software to align with customer needs, providing qualification documentation in compliance with pharmaceutical regulations.



**Tempris technology with battery-free and wireless sensors is the GOLD STANDARD in temperature measurement during lyophilization. With compliance to 21CFR Part 11 (FDA) and GAMP 5 (EMA) regulations, it ensures full data integrity for GMP applications and is one of the most reliable methods available**

### Tempris System Components: A Holistic Overview

The Tempris system comprises temperature probes situated within vials or other product containers, an array of antennas within the lyophilizer, an interrogation unit connected to the antennas via cables, and a computer linked to the interrogation unit.

At the core of each Tempris probe lies a meticulously shaped and mounted quartz crystal. These crystals exhibit the piezoelectric property, causing them to oscillate in response to the applied voltage, with the frequency of oscillation dependent on the temperature. Once the excitation energy ceases, the piezoelectric property prompts the crystal to generate an electric field, empowering each probe to transmit a return broadcast encoded with temperature information.

Optimal antenna placement within the lyophilizer facilitates the transmission of the excitation signal to the probes and the reception of the return signals multiple times per second. This allows for the digitalization of product temperature data, enabling comparison and improvement processes.

### The Gold Standard in Temperature Measurement

"Tempris technology with battery-free and wireless sensors is the gold standard in temperature measurement during lyophilization. With compliance to 21CFR Part 11 (FDA) and GAMP 5 (EMA) regulations, it ensures full data integrity for GMP applications. Its accurate measurement process, free from heat input, and real-time transmission of data make it one of the most reliable methods available," says Jim Searles, Ph.D., technical advisor, and representative.

A contract manufacturer in Europe, producing a global company's lyophilized product, has successfully employed

Tempris sensors in over 160 batches. Embracing the continuous process verification (CPV) approach, they have not lost a single batch due to lyophilization issues, crediting the reliability of Tempris data in ensuring acceptable product temperatures during deviations. This remarkable performance has allowed the customer to include Tempris data evaluations in regulatory filings, securing regulatory flexibility for process modifications and equipment changes. The commitment to continuous data evaluation has granted them the freedom to adapt their process for different batch sizes, cycle modifications, and equipment transitions across multiple global markets.

### Team Dynamics and Global Collaborations

The company has around 30 members and organizes its operations into separate teams for sales and service. Tempris is ISO qualified, conducts in-house manufacturing, and serves clients worldwide, including the USA, Japan, Korea, Taiwan, India, and Europe with a focus on client understanding and process improvement.

Tempris has established its technology across diverse industries and boasts a clientele of 20 major pharmaceutical companies, CMOs, CDMOs, and laboratories. It has successfully implemented the technology in approximately 250 projects globally, offering support for various primary packaging formats. Collaborating with ATS (formerly SP Scientific), it integrated the Tempris system into high-end development and commercial freeze dryers.

Today Tempris is a revolutionary tool in the field of lyophilization for pharmaceutical applications. This is attributed to its ability to shift focus from mere validation to the continuous monitoring of critical quality attributes during lyophilization processes.

"With Tempris technology, we now have the capability to conduct critical quality attribute monitoring anywhere in the equipment—a crucial aspect that, until now, lacked scientific understanding. This advancement allows the user to gather comprehensive data and establish connections within the full-scale equipment, enabling our customers to enhance product quality, increase throughput, and bolster the reliability of the entire process," says Anton Mangold, CEO of Tempris GmbH.

Tempris technology is a pivotal tool in simplifying the regulatory approval process, offering a streamlined approach to continuous data collection on the most critical parameter in freeze drying. By providing an in-depth understanding of the process, it facilitates a smoother regulatory approval journey for companies. "Tempris goes beyond conventional monitoring systems by offering the ability to monitor and control data across multiple freeze dryers and sites, even on an international scale. In essence, it enhances data accuracy and contributes to a more efficient and globally adaptable regulatory compliance experience for companies venturing into freeze-drying applications," concludes Dr. Hansjoerg Hufnagel, head of sales, marketing & BD. 