



*Customized GMP
Freeze-Drying Solutions*

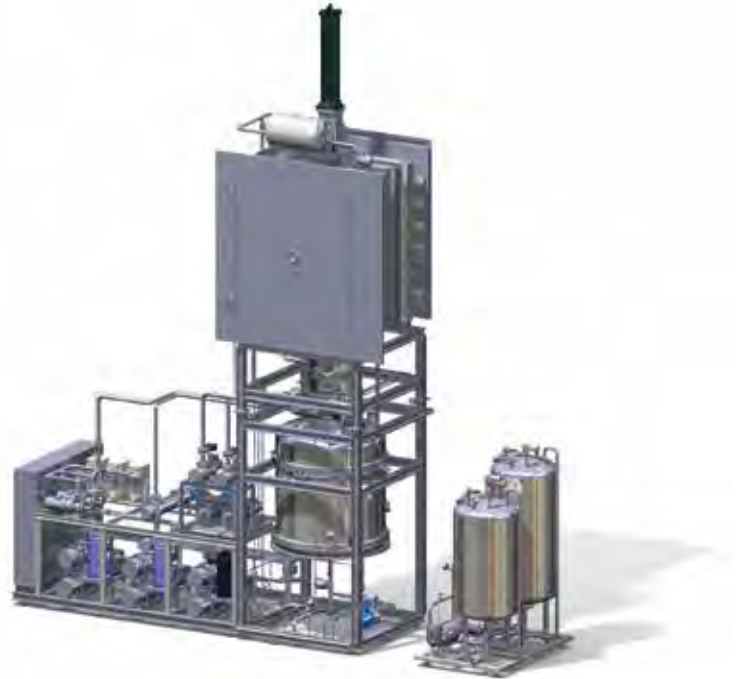


Challenges made easy through expertise and innovation

The main challenges in today's generic and specialty drug and biotech markets are shortening time to market and increasing productivity while assuring quality and reducing costs. Freeze-drying is not a novel technology by any means and the pharmaceutical industry, influenced by safety and validation requirements has introduced policies that tend to restrict process improvements. The focus of the industry has been focused on repeatability of the same process, and knowledge on how the process affects the product has had lesser importance providing the quality is assured. Under these circumstances, the most appropriate approach to reduce cost is through reduction in cycle times.

TELSTAR works in partnership with clients to develop the most appropriate solution, offering reliable and trouble-free process technology based on many years of experience working with the pharmaceutical and biotech industries across a variety of pharmaceutical applications.

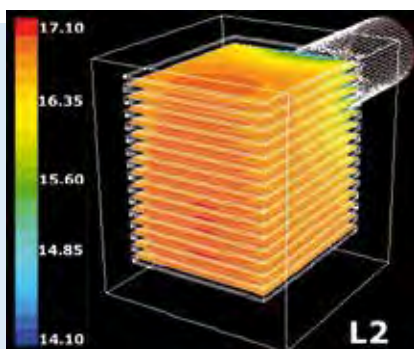
TELSTAR recognises that the quality of engineering design, components, and workmanship will define the finished product. **TELSTAR's** innovative approach to engineering design includes the in-house developed **Lyodynamics** finite element simulation software to study the chamber-condenser arrangement design to provide the best flow pattern. Given the operating conditions (sublimation rate, temperature and operating pressure) and the geometry of the equipment, it is possible - by means of CFD - to calculate the local conditions (pressure, gas velocity, ice deposition, etc) in the drying chamber, the duct and the ice condenser. Powerful analytical correlations have been developed that can predict and extrapolate the effect in the process of other configurations, varying design parameters (chamber, shelf interdistance, duct, etc) and/or operating conditions. Through this type of technology, **TELSTAR** has acquired a comprehensive fundamental



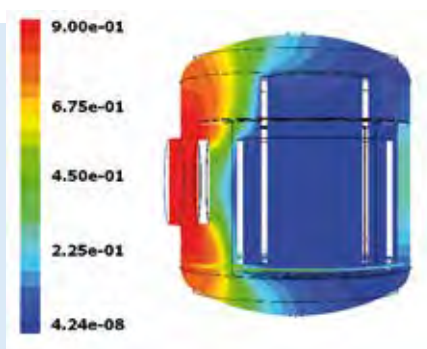
knowledge of how to improve freeze-drying processes through equipment design.

Integrating various core technologies, **TELSTAR** provides turn-key custom-made solutions to solve a customer's most challenging applications. To ensure the equipment fully satisfies requirements, **TELSTAR** undertakes factory acceptance testing (FAT) of all freeze-dryers, simulating as closely as possible real working conditions.

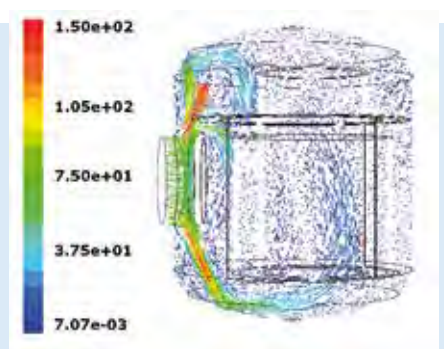
In essence, excellent engineering coupled with efficient manufacturing and business practices provides high quality solutions at superior value. **TELSTAR** is constantly developing solutions to address emerging challenges in pharmaceutical freeze-drying technology.



Contours plot of the absolute pressure over the plates in a Lyomega 400.



Contours of water mass fraction in a vertical condenser.



Contours of the velocity vectors of the gas mixture in a vertical condenser.

for Pharmaceutical Production



Lyosuite™

21 CFR part 11 compliant control system based on PLC and user friendly SCADA

TELSTAR understands that precise control and reproducible results are key to efficient production. Moreover, loss of product can represent substantial value. For this reason, a Programmable Logic Controller (PLC), with proven reliability, is the process controlling device.

TELSTAR engineers developed the **Lyosuite™** control system with these principles in mind. **Lyosuite™** is a Supervisory Control and Data Acquisition (SCADA) system integrated with an innovative suite of process tools. Engineering practices are consistent with current Good Automated Manufacturing Practices (cGAMP) and result in a precise, stable control system that comprehensively addresses a client's process control and validation requirements.

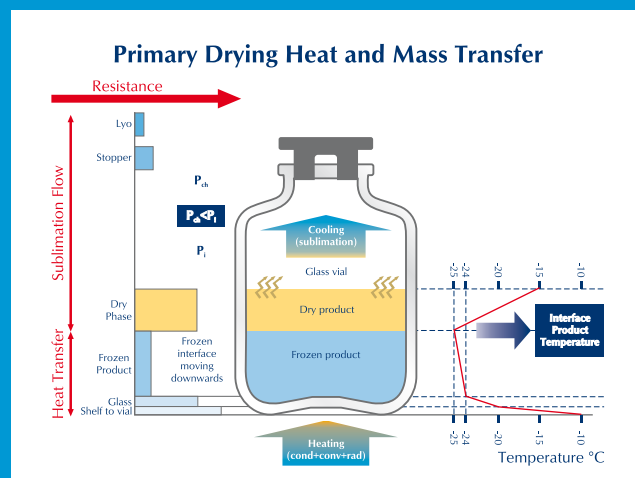
The **Lyosuite™** system offers multitasking operation in a Windows® environment. In addition to the supervisory control and data acquisition functions, it provides compilation and editing of complete recipes, including linking of ancillary cycles (CIP, SIP, filter integrity testing or vial stoppering) to the freeze drying cycle. Help is interactively provided through pop-up windows.

Customized control architectures to provide redundancy or to integrate with a client's IT infrastructure, policies and specifications are available.



Lyometrics and Lyodriver

TELSTAR has completed the development of the Lyometrics software module, a 'sensorless' process parameters measurement program that can be implemented in **Lyosuite™** SCADA control systems of new freeze dryers. The Lyometrics is an innovation through which advanced freeze-drying process information can be obtained, which in turn provides knowledge on how the process can be improved. Lyometrics, a non-invasive monitoring technique, is a valuable alternative to classical temperature sensors by enabling quantification of the variables which are of the utmost interest during primary drying: sublimation interface temperature and sublimation mass flow. Additionally, this technique measures the heat transfer and the mass transfer coefficients.



The method introduces a small perturbation in the process and the system response to this perturbation is acquired. A set of equations describing the process mathematical model are then solved in order to 'reproduce' the system response.

All **TELSTAR** lyophilizers are ready-prepared to integrate the Lyometrics as an option. A step further is the Lyodriver, which will be the first software to control a lyophilization process via a PAT (Process Analytical Technology) approach.

Integrated and Customised Solutions

Isolation and containment solutions

TELSTAR's in house expertise and manufacturing capabilities in isolation technology solutions facilitates a perfect integration of systems for containment or aseptic applications.



1. Bulk freeze-dried product vacuum unloading operation through isolator.
Containment: $< 1 \mu\text{g}/\text{m}^3$

2. Freeze-dryer containment isolator.
Containment: $1 \text{ ng}/\text{m}^3$

Freeze-drying development support laboratory

The emergence of biotechnology and the resulting production of protein-based therapeutic agents have increased the importance of freeze-drying process technology. This technology offers significant advantages such as:

- Dosage form stabilisation
- Accurate dosage vial filling
- Rapid dissolution of the freeze-dried product
- Sterility of the manufacturing process

However, as with any other technique, process characteristics should be carefully considered in any formulation intended for injection. Both the freezing and drying processes can impose stresses that may result in the inability to recover activity following reconstitution of the dried solid to liquid form. In many instances this issue can be overcome by appropriate choices of the formulation and the freezing and drying process conditions.

A fully equipped freeze-drying support laboratory is available for TELSTAR's customers to determine the thermal properties of the product or to develop optimised freeze drying cycles. Freeze-drying fundamental training programs are also available.

Cryogenic microscope for determination of glass transition point.



Integrated and Customised Solutions for Pharmaceutical Production

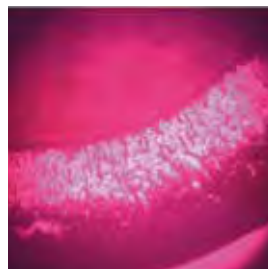


*Loading and
unloading systems*

*Freeze-drying
systems*



*Freeze-drying
development
support laboratory*



*Bulk filling /
off loading
systems*



*Isolation and
containment
solutions*



Project Management

Each project is handled by a project team consisting of a project manager that coordinates communication between the customer and the rest of the project team; a mechanical design engineer, a control design engineer, a validation engineer, a manufacturing engineer and a logistics engineer.



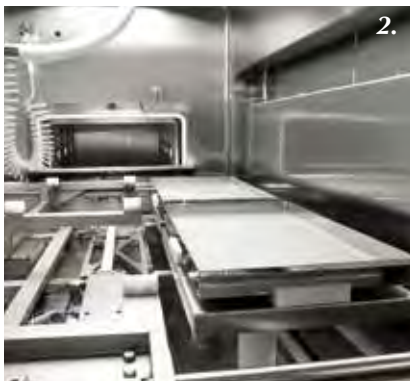
Integrated and Customised Solutions

Loading and unloading systems

The Lyogistics range of freeze-dryer loading/unloading solutions covers a complete range of vial and bulk applications from manual through semi-automatic to fully automatic systems to meet the requirements of each project. Technologies include the use of anthropomorphic robots for handling of trays, vacuum-based bulk powder unloading systems, tray-less 'fixed' row-by-row or 'flexible' shelf-by-shelf vehicle systems.



1.



2.



3.

1. Lyogistics RxRLUS 400 push-in / push-out row by row vial automatic loading / unloading system.

2. Lyogistics TLUS 900 bulk tray semi-automatic loading / unloading system integrated with isolator.

3. Lyogistics FLUS 1500 push-in / pull-out row by row frame vial semi-automatic loading / unloading system.

Bulk filling / off loading systems

TELSTAR also offers solutions for bulk filling of dried product into drums or intermediate bulk containers (IBC) and the off loading and packaging of the dried product from IBC into smaller containers.

Lyogistics FABS 1500 bulk automatic loading/unloading system.

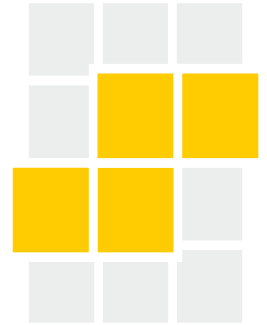
The system uses tilting shelves and includes automatic dosing of the product solution and an anthropomorphic robot for automatic unloading of dried product.



for Pharmaceutical Production

Freeze-drying systems

TELSTAR offers design flexibility to address the requirements of each project. Customisation capabilities cover a wide range of engineered solutions, including two-door pass-through design and sub-doors for product loading and unloading at a constant level. Internal or external condenser systems can be in horizontal or vertical configurations and can be positioned adjacent to or below the chamber. Refrigeration systems range through double stage or cascade reciprocating compressor, screw compressor or liquid nitrogen and a full range of customised CIP systems is available.



*Lyomega 80 ST LN₂;
Pass - through chamber,
liquid nitrogen refrigeration
system, mushroom
type chamber - condenser
isolation valve, integra-
tion with isolator and
continuous shelf interdis-
tance adjustment system...*



*From
3D design
to
as built*



Services

Preventive Maintenance Programs

Routine maintenance is an integral part of **TELSTAR's** cGMP approach. All maintenance activities are properly documented to provide support during corporate audits and regulatory inspections. A preventive maintenance program will assure compliance and continuity of validated equipment status, maintain equipment reliability, minimise downtime and extend the equipment life-span.

Validation support

Engineering and manufacturing practices follow ISO 9001:2000 quality standards and the cGAMP (Good Automated Manufacturing Practices) guidelines. Design Qualification (DQ), Installation Qualification (IQ) and Operational Qualification (OQ) testing and comprehensive documentation are standard **TELSTAR** practices. The aim is to make on site validation faster, easier and efficient.

Calibration services

Calibration must fulfil both maintenance and compliance requirements. **TELSTAR** can develop a comprehensive program to gain direction for classifying instruments and setting appropriate limits to ensure product quality and avoid unnecessary deviation investigations. **TELSTAR** can provide calibration procedures and perform calibration of instruments using highly qualified technicians and fully traceable primary instruments.

Training services

A wide range of training programs is provided for machine operators, electrical and mechanical engineers, maintenance engineers and supervisory personnel. The programs are designed not only to improve the participants' overall understanding of the production equipment, but also to enhance their confidence and performance levels to provide a beneficial return for the business.

Upgrades & refurbishment

TELSTAR's Customer Service organization provides a wide range of refurbishing services: popular examples being control system upgrades, refrigeration and vacuum system improvements and retrofit of filter integrity testing.



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