



FREEZE DRYER SMH RANGE
The production freeze dryers for
Pharmaceutical and Biotechnology industries



USIFROID BACKGROUND



USIFROID is recognised as a world leader in freeze drying technology with a reputation for quality worldwide.

For over 60 years **USIFROID** has been manufacturing freeze drying and associated equipment both for industrial and research applications.

In the specialized field of pharmaceutical and biological products, **USIFROID** enjoys an international reputation for quality, choice, flexibility and technology.

Located 30 km south west of Paris, **USIFROID** exports a significant part of its activity and is represented in over 30 countries worldwide.

As a Telstar Group company, **USIFROID** offers real stability and strength to innovate constantly.

WHAT USIFROID OFFERS

- A wide range of freeze dryers and associated equipment that can be customised to meet your exact requirements.
- A project management concept, to assure close control during order execution while maintaining good communication, on-time delivery, quality and performance.
- A broad experience in the design of sterile applications to meet cGMP and all regulatory guidelines.
- The ability to engineer and manufacture large and complex systems involving associated pieces of equipment such as freezing tunnel, central refrigeration group, automatic loading and unloading systems, storage chambers, isolators, etc.
- A range of research and pilot-scale freeze dryers manufactured to the same state-of-the-art quality standards as the industrial units and available with all the accessories to allow easy scale-up.
- Validated and proven control systems designed and tested by a group of experts with extensive knowledge of the lyophilisation process.
- State of the art quality of manufacture for reliable and long lasting machines.
- A large team of experienced technicians to help you with maintenance and support trouble-shooting operations.

In the world of freeze drying, **USIFROID** has unrivalled experience with 60 years of steady growth and an international reputation for excellence. **USIFROID** is the vendor with all the assets to give you confidence for the next 20 years.

FREEZE DRYER SMH: A MODULAR RANGE

To meet the great variety of needs from its customers, **USIFROID** has designed its production freeze dryers following the modular concept: each machine is an assembly of pre-tested modules which are based on proven technologies and designs.

Freeze dryers have been divided into different parts, for which standard modules have been developed:

- Chamber and shelves
- Condenser
- Refrigeration system
- Vacuum system
- Electrical panel and control system

Using fully integrated computer aided design, the whole freeze dryer is rapidly defined. This way, **USIFROID** can build in minimum time a reliable freeze dryer which fully matches the customer's requirements. The SMH modular range is also the best solution to accommodate specific layout arrangements while maintaining an easy access for the maintenance.

In addition to these standard modules, some applications may require specific development related to the lyophilisation process or to the environment of the freeze dryer. Based on its modular range of products, **USIFROID** can propose fully engineered solutions to match special requirements.

VALIDATION

Validation starts at the very beginning of every project with Design Qualification. Test Master Plans for FAT and SAT are produced. Then, standard or customised protocols for SQ (software qualification), IQ and OQ are prepared and approved by the customer. **USIFROID** can perform full validation on site.

USIFROID freeze dryers are designed and manufactured to meet the cGMP and all the relevant regulatory guidelines.

QUALITY CONTROL

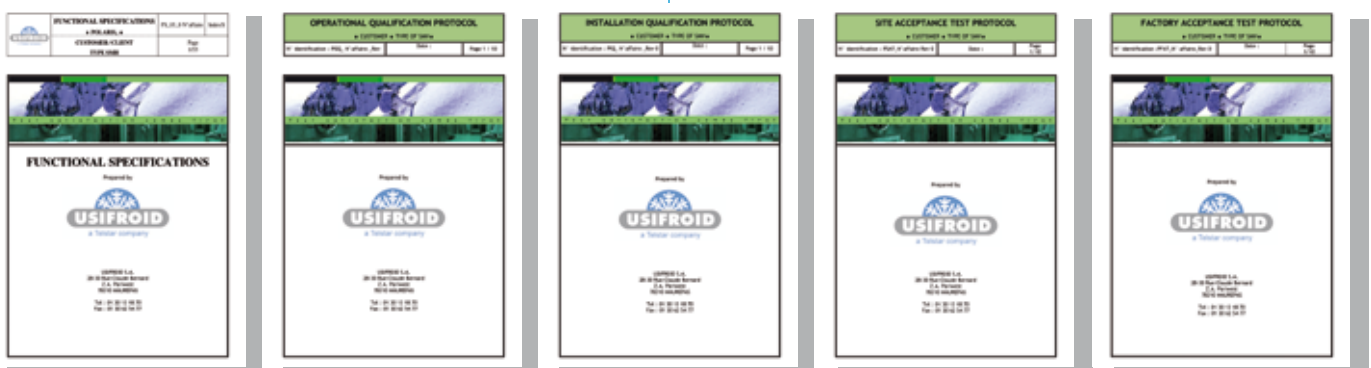
All the installations are fully assembled and tested prior to shipment. A comprehensive FAT programme is submitted to the client for approval. Where possible the freeze dryers are installed in the factory to follow exactly the final layout.

Full design, installation and operational qualification support can be executed in the presence of client's representative.

MAINTENANCE

USIFROID pays close attention to details in order to eliminate costly maintenance problems. The design of the freeze dryer takes into account the space available and operational constraints.

USIFROID only uses components and parts from international first class manufacturers in order to reduce costly spare parts stock and ensure compatibility. Every component of the freeze dryer is tagged and traceable to the component list and P&ID to provide easy maintenance and trouble-shooting.



CHAMBERS & DOORS



QUALITY AND SAFETY

All **USIFROID** chambers are built to meet local codes and regulations. Insulation and door interlocks are designed for operator protection against excess temperature and pressure. **USIFROID** performs Risk Analysis for operator safety on every freeze dryer.

ADAPTED TO A STERILE ENVIRONMENT

Great attention is made to the details to avoid crevices and ensure cleaning and sterility. Connection ports are designed to avoid dead-legs. Insulation is sealed for high performance and long life, stainless steel cladding panels provide robust, pharmaceutical grade, external finish. Low friction hinges are designed for easy opening, even on largest doors. Dual gasket system eliminates friction on locking devices.

FLEXIBILITY

Doors are usually hinged, with manual or automatic locking. Sliding type is also available. **USIFROID** can provide double ended or «pass-through» systems enabling easier maintenance and optimised production. Loading and unloading is also feasible through a slot «pizza» door. The slot «pizza» door greatly improves product protection and reduces condensation when loading on pre-cooled shelves.



SHELVES & STOPPERING

STOPPERING

USIFROID offers two alternatives of stoppering systems: hydraulic or screw type. Variable shelf spacing is available with both alternatives.

• Hydraulic type: 2 versions

- Hydraulic stoppering system is of «bridge» design, which ensures that no non-sterile component enters the chamber before the vials are fully stoppered. The stoppering operation is bottom-up.

- Hydraulic stoppering system is of «central» design, which ensures that no non-sterile component never enters the chamber. The stoppering operation is up-bottom. This system allows loading/unloading at low or constant level.

The possibility of hydraulic fluid leaking into the drying chamber is completely eliminated.

• Screw type

This revolutionary patented design operates by using two helical screws driving an upper reinforced plate to which the shelves are suspended. No components enter or leave the chamber during operation.

As there is no hydraulic piston, no excessive height is needed in the machine room. All the components are non particle shedding and are sterilised with the chamber.

Loading at a constant level is possible.

The system positions shelves very accurately, which is critical for automatic loading systems. The shelf movement is very smooth, which prevents risk of falling, in particular for high unstable vials or ampoules. No other stoppering system can offer all these advantages. Most of **USIFROID** lyophilisers are delivered for high-technology applications requiring cleaning and sterilisation.

SHELVES

• Quality

Heavy gauge construction means confidence for life, even with routine stoppering. Flatness is assured to 1 mm/m to provide perfect contact with trays or vials. Temperature distribution within $\pm 1^{\circ}\text{C}$ to ensure uniformity of every batch, even on the largest machines.

• Flexibility

User friendly repositioning system ensures shelf area is maximised to match every size of vial. Shelf spacing options are calculated to optimise the overall capacity.



STERILISATION AND CIP CLEAN-IN-PLACE

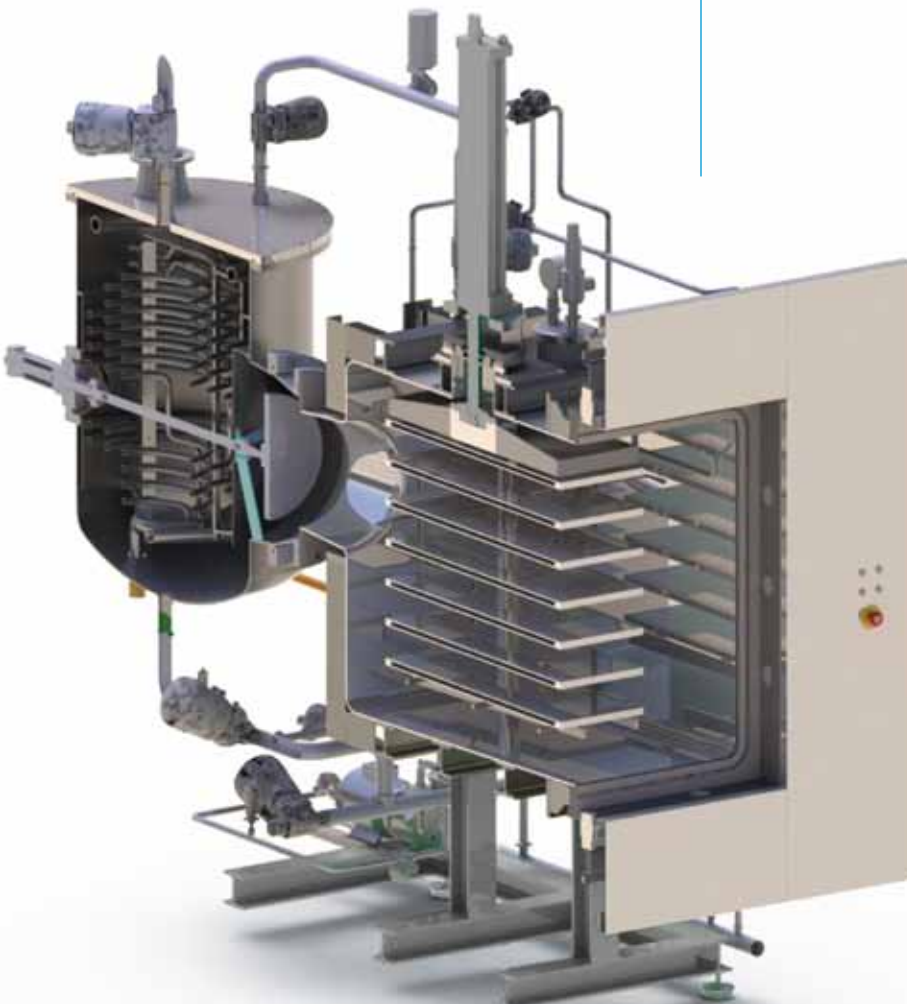
CLEAN-IN-PLACE

USIFROID offers several approaches to clean its freeze dryers.

- Using high flow steam condensation alone, which ensures a real and overall cleaning effect, that can be validated.
- Using a spraying manifold with nozzles and spray balls, to spray water (WFI) and cleaning solutions, on the internal surfaces of the chamber and condenser. Recirculation is possible to limit water consumption.
- **USIFROID** has always used liquid-ring vacuum pumps for air removal and drying related to sterilisation and cleaning operations. This is now a standard in the industry.
- Included in the standard package is the air/nitrogen inlet filter with the valve manifold permitting in-situ integrity testing. Built-in automated integrity test can also be offered.

STERILISATION

- **USIFROID** chambers are steam sterilisable and pressure vessels are built according to codes and regulations applicable in the country where the machine will be installed.
- Great care is taken to eliminate cold spots and dead legs in pipe-work. This is backed up by intensive validation studies.
- **USIFROID** chambers are designed to be fully drainable, and the drain is easily accessible from the door.



PROCESS CONDENSERS

- **Flexibility**

USIFROID is unique in offering maximum flexibility for the location of the condenser. The condenser can be internal or external and positioned behind, on the side, above or below the product chamber. No other manufacturer can offer a top mounted condenser with stoppering.

Ice capacity range from 20 to 800 kg.

- **Efficiency**

High efficiency vertical coil design with truly independent multiple circuits and dedicated compressors. This design has proven to be very efficient in preventing oil back-streaming from the vacuum pumps.

Plate type designs are available for special applications.

- **Technology**

No dead areas as in horizontal designs.

The condenser design minimises compressor lubricating oil trapping in the coil and therefore increases compressors up-time.

USIFROID uses only the best separating valves, either butterfly type with long lasting seal positioned in a vacuum jacketed groove or mushroom type used on top mounted condensers.

VACUUM SYSTEM

USIFROID offers a choice of vacuum systems, from recognised manufacturers.

- Oil lubricated or dry pump
- Dual pump system, to decrease initial vacuum time and provide redundancy
- Roots booster pump



HEAT TRANSFER SYSTEM

LIQUID NITROGEN

USIFROID offers a real alternative to conventional refrigerants with proven low-temperature technology.

Liquid nitrogen can be used either as a low-temperature solution, for example to trap organic solvents, or as the main cooling medium for both the shelves and the condenser.

The advantages of liquid nitrogen are as follows:

- Better reliability
- Eliminates costly maintenance on compressors
- Eliminates the needs for electricity and cooling water for compressors
- Cooling power is constant throughout the temperature range
- Reduces the space needed for the installation
- Eliminates noise problems

HEAT TRANSFER SYSTEM

• **Simplicity**

The entire system is designed to avoid the need for filters, driers, relief valves and other devices which are a source for maintenance problems.

• **Flexibility**

USIFROID propose the choice between reciprocating compressors, screw compressors with non CFC refrigerant, and liquid nitrogen cooling system.

• **Technology**

USIFROID was first to deliver a large industrial lyophiliser using liquid nitrogen technology only. Central refrigeration systems are also available to reduce costs on large installations.



LOADING SYSTEMS - SPECIFIC APPLICATIONS

SPECIFIC APPLICATIONS

USIFROID can provide custom design for every application, whether for bulk product, vials or ampoules.

USIFROID has experience in automatic or semi-automatic loading solutions with:

- Loading at constant level
- Loading shelf by shelf
- Pass-through or single door solutions
- Intermediate storage before and after lyophilisation
- Loading with or without trays
- Protective environments during loading / unloading in an isolator or under laminar flow

USIFROID's solutions always prefer simple and safe movements, with each device assuring one single movement.

Particular attention is paid to allow easy cleaning of the system and avoid particle generation.

Some applications require a specific development related to the lyophilisation process or the environment of the freeze dryer. Based on its modular concept, **USIFROID** can propose fully customised installations.

In such case, **USIFROID** follows specific procedures in order to validate the chosen technical solutions.

Here after are some of the specific projects realised by **USIFROID**:

- Products with special conditioning requiring to adapt the inside arrangement of the freeze dryer
- Central refrigeration system, to supply several freeze dryers
- Freeze dryer built for explosion-proof environment
- Installation of freeze drying units on several levels
- Extreme technical performance (very cold temperature, fast cool down rate...)
- Very large capacity
- And many more...



CONTROL SYSTEMS

Control system is another area where **USIFROID** is a world leader.

- **Development under control**

USIFROID designs its control system following the principles of the GAMP.

A Functional Requirement Specification (FRS) is written by **USIFROID** specialists based on the User Requirement Specifications (URS). Once the FRS is approved by the customer, the Functional Analysis (FA) is written. It defines in details all functions and actions the controls system needs to perform. From this stage, the software code is developed and documented accordingly, in a controlled manner, according to procedures stated in USIFROID Quality Assurance system.

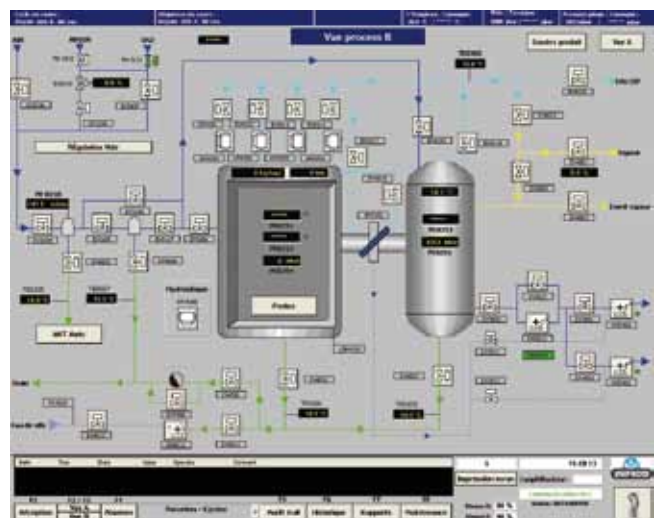
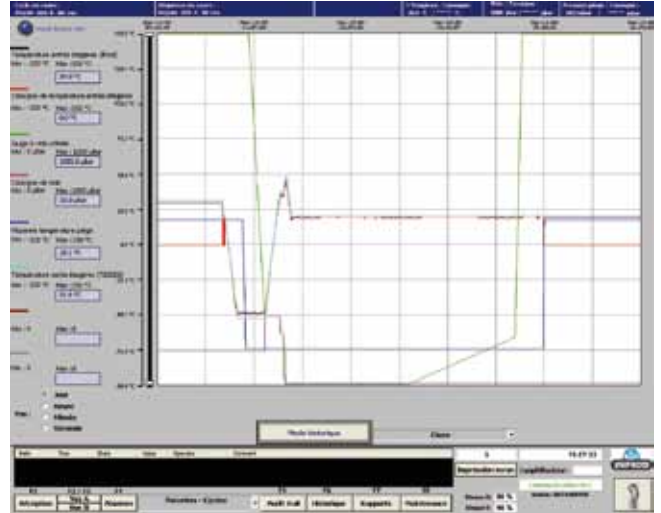
- **Maintenance**

As a freeze dryer is built to last, USIFROID designs its control system so that they can be maintained over the years. Evolution is possible, in order to follow the ever changing requirements of the industry.

POLARIS

An open system, based on a PLC process controller and PC human machine interface compliant to 21 CFR part 11 regulations, using commercial hardware and software packages frequently used in the pharmaceutical industry.

USIFROID has validated this architecture on Allen Bradley and Siemens PLC and on Intouch SCADA systems. Therefore the customer is able to choose the right combination. If required, all source codes and complete documentation can be provided. So the system would totally belong to the customer.



TYPICAL COMBINATION FOR MODULAR LYOPHILISER

Model number SMH	162	243	324	378	540	648	1188	1440	1800	1980	2340	2700	3240	4050	4590
Type of chamber	O	O	O	O	O/□	O/□	□	□	□	□	□	□	□	□	□
Shelf area (m ²)	1,62	2,43	3,24	3,78	5,4	6,48	11,8	14,4	18,0	19,8	23,4	27,0	32,4	40,5	45,9
Shelf width (mm)	450	450	600	600	900	900	900	1200	1200	1200	1200	1500	1500	1500	1500
Shelf length (mm)	900	900	900	900	1200	1200	1200	1500	1500	1500	1500	1800	1800	1800	1800
Number of shelves	4	6	6	7	5	6	11	8	10	11	13	10	12	15	17
Nominal ice capacity (kg)	40	40	60	60	100	100	200	200	300	300	400	600	600	800	800

Other dimensions are available, as needed

SERVICES REQUIRED

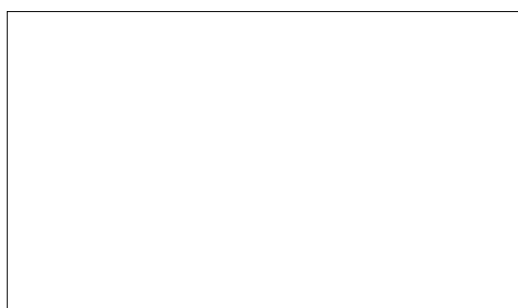
- 3-phase electrical power
- Water for compressor cooling and/ or liquid nitrogen when «cryogenic lyophiliser» option
- Hot water or steam for de-icing
- Compressed air for valve actuation
- Air/N₂ for vacuum release
- Water for CIP
- Steam for sterilisation

CHARACTERISTICS

- Shelf temperature: -55 / +80°C (with R404A)
- Condenser minimum temperature: -80°C (with R404A)
- Nominal vacuum limit: 5 to 20 µbar
- Typical pumping time to 100µbar: 20 to 30 minutes
- Silicone oil 5 cst used as circulating thermal transfer medium
- Typical electrical heating resistance: 1.5kw/m² of shelf
- Main compressor(s) used for shelf or condenser cooling
- Typical refrigerants: R404A, R507F
- Leak rate of the assembled system: (1x10⁻² mbar x litre/second)

OPTIONS (for client to specify)

- Internal/external process condenser
- Type of door: hand-wheel / peripheral locking / sliding
- 316L stainless steel or better
- Polishing: Ra 0,5 µm
- Screw compressor
- Auxiliary compressor used for fine adjustment of shelf temperature during sublimation
- In lieu of the compressors, or in order to ensure a back-up, «cryogenic» configuration: the cooling-down is obtained by liquid nitrogen
- Liquid nitrogen cooling as main source or as back-up
- Stand-by vacuum pump / «Chemical» type / dry pumps / roots blower / pump protection filter
- Dual circulating pumps
- Sterilisation by steam 123°C or higher
- In-line sterilising filter 0.2µ, with valving for integrity test / built-in integrity test
- Stoppering (hydraulic or screw)
- Clean-in-place (CIP)
- POLARIS control and regulation with PLC (Siemens, Allen Bradley) with H.M.I. (configured with InTouch)
- Vacuum pump filter protection
- Drain recovery and treatment tank



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