

Glossary of Freeze Drying Terms



PRECISION FREEZE DRYERS MADE IN THE USA

- **Laboratory**
- **Pharmaceutical**
- **Industrial**
- **Benchtop**
- **Floor Models**
- **For Clinical, Production & General Use**

Amorphous

Amorphous material usually consists of compound materials that do not become crystalline when frozen, do not have a eutectic point and turn into a “glass.” Amorphous solids are non-crystalline; translational periodicity or “long range order” is absent. Freeze drying for amorphous mixtures is normally performed below the glass temperature.

Annealing

Annealing is the process of cycling a product below and then above its final freezing temperature (below its triple point) to enable crystallization.

Backstreaming

Backstreaming is a potential source of water and hydrocarbon vapor contamination migrating from a vacuum pump.

Blank-Off Pressure

This is the ultimate pressure the pump or system can attain.

Bound Water

Bound Water usually refers to water that is an essential component to various materials, distinguishable from free water by its inability to form ice crystals. Unbound or “Free Water” is removed from the material with a second step of heating used to remove “Bound Water” thereby producing the driest possible end-product.

Breaking Vacuum

Admitting air or a selected gas to an evacuated chamber, while isolated from a vacuum pump, to raise the pressure towards, or up to, atmospheric.

Cake

Also sometimes referred to as a “plug,” cake is the product resulting from lyophilization.

Collapse

Collapse can happen when material reaches a temperature (called the ‘collapse temperature’) that causes the product to soften to the point of not being able to support its own structure.

Condenser

The Condenser also called a “Cold Trap” is a chamber that captures water and other solvent vapour by providing surfaces for their re-solidification.

Circulation Pump

A pump for conveying the heat transfer fluid.

Conax Connection

A device to pass thermocouple wires through and maintain a vacuum tight vessel.

CPP

Freeze Drying occurs in stages of freezing product below its triple point and then drying the product through both sublimation to remove “free water” and desorption to remove “bound water.” The correct rates for each stage of the process may be referred to as “CPP” or Critical Process Parameters.

CQA

Critical Quality Attributes (CQA) are chemical, physical, biological and microbiological attributes that can be defined, measured, and continually monitored to ensure final product outputs remain within acceptable quality limits.

Critical Temperature:

The critical temperatures in freeze drying are 1) T_c - Collapse temperature 2) T_{eu} - Eutectic temperature and 3) T_g' - Glass transition temperature

Crystalline

A crystal or crystalline solid is a solid material whose constituents are arranged in a highly ordered microscopic structure, forming a crystal lattice. In practice, the crystalline form is produced at any stage of the lyophilization process (i.e. freeze concentration, primary drying, anealing, secondary drying.)

DQ

The DQ (Design Qualification) process and documentation is used to describe the lyophilizer’s engineering and construction for meeting the User Requirements Specifications (URS).

Desiccant

A drying agent.

Desorption

After the first stage of removing water by sublimation, remaining water that is considered “bound” or “absorbed” is removed in a second stage of freeze drying also called the “desorption phase” by raising shelf temperature and reducing chamber pressure to a minimum.

Eutectic Temperature

The Eutectic Temperature is the temperature below which no liquid solution phase exists in equilibrium with any crystalline phase. Only two phases, liquid and solid are in equilibrium at the eutectic temperature.

Factory Acceptance (FAT)

The Factory Acceptance Test (FAT) is a project milestone where the equipment and/or system integrator demonstrates that the system design and manufacturing meets the contracted specifications.

Foreline

The exhaust of the pump called the “foreline” which carries the solvent vapor (mainly water vapor) to the condenser.

Free water

Free Water is the water that is formed into crystals and removed during the first phase of freeze drying called sublimation. Bound water, distinguishable from free water by its inability to form crystals is removed in the second phase of freeze drying called desorption.

Glassy state

Amorphous, multi-component mixtures which do not crystallize and do not have a eutectic point turn into a “glassy state.” Few products are simple crystalline materials, the vast majority of products that are lyophilized are amorphous and form glassy states when frozen.

Hygroscopic

A substance tending to take on moisture from the air under some conditions of humidity and temperature is “hygroscopic.”

Inspection Qualification (IQ)

An inspection process that qualifies every aspect of the freeze dryer against its manufacturer's specifications.

Leak Rate

Leakage into a lyophilizer may originate from various sources. As in any vacuum chamber, leakage can occur from the atmosphere into the vessel itself. The Leak Rate is the measurement of leakage.

Melt-back

Unbound moisture and/or solvent not completely removed during the sublimation phase can cause the product to collapse or melt back. Understanding the glass transition temperature and collapse temperature a conservative lyophilization cycle can be run involving the various states of freezing, annealing (if necessary), freezing, primary drying to avoid melt-back.

Non-Condensables

A mixture of gases such as nitrogen, hydrogen, chlorine, and hydrocarbons. They may be drawn into the system through leaks when part of the system is under a vacuum. Their presence reduces the operating efficiency of the system by increasing the condensing pressure.

Nucleation

The formation of ice crystals on foreign surfaces or as a result of the growth of water clusters.

Oil-Mist Filter

In vacuum terminology a filter attached to the discharge (exhaust) of an oil-sealed rotary pump to eliminate most of the "smoke" of suspended fine droplets of oil which would be discharged into the environment.

Oil Sealed Rotary Pump

A standard type of mechanical vacuum pump used in freeze-drying with a high compression ratio but having a relatively low displacement (speed) for its size. A two-stage pump is effectively two such pumps in series and can obtain an ultimate vacuum.

Oil Separator

Separates the oil from the compressor discharge gas and returns the oil through the oil float trap and piping to the compressor crankcase.

Operational qualification (OQ)

The process that verifies that a vacuum freeze dryer effectively handles the through put requirements specified.

Real leak

A real leak is a source of atmospheric gases resulting from a penetration through the chamber.

Reconstitute

The dissolving of the dried product into a solvent or diluent.

Relief Valve

Used for safety purposes to prevent damage in case excessive pressure is encountered.

Rotary Vane Pump

A mechanical pumping system with sliding vanes as the mechanical seal. Can be single or two stages.

Shelf Compressor (Controlling Compressor)

Used for controlling the shelf temperature, either cooling or from overheating.

Shelves

In terms of the lyophilization process, they are a form of heat exchanger, within the chamber, that have a serpentine liquid flow through them, entering one side and flowing to the other side. They are located in the circulation system.

Self Liquid Heat Exchanger

The transfer of heat from the shelf fluid to the refrigeration system through tubes in the exchanger causing compressor suction gas to warm.

Single Stage Compressor

This is a normal type compressor used in refrigeration. In the lyophilization process it is used to control the shelf temperature, both for cooling and keeping the shelf temperature from overheating using a temperature controller.

Silicone Oil

A heat transfer fluid.

Site Acceptance Test (SAT) / Factory Acceptance Test (FAT)

A FAT or Factory Acceptance Test is usually performed at the vendor prior to shipping to a client. The vendor tests the system in accordance with the clients approved test plans and specifications to show that system is at a point to be installed and tested on site. A SAT is a Site Acceptance Test where the system is tested in accordance to client approved test plans and specifications to show the system is installed properly and interfaces with other systems and peripherals in its working environment.

Sterilization

The use of steam and pressure to kill any bacteria that may be able to contaminate that environment or vessel.

Sublimation

The sublimation event is the transition of water / solvent from a solid to gas phase, occurring when all components (tissues, interstitial matrix, water, etc.) are solidified and maintained at a temperature below their glass transition temperature or crystal melt temperature, whichever is lower.

Suction Line Accumulator

To provide adequate refrigerant liquid slug protection (droplets of liquid refrigerant) from returning to the compressor, and causing damage to the compressor.

TCE

Trichloroethylene - A heat transfer fluid.

Thermocouple

A metal-to-metal contact between two dissimilar metals that produces a small voltage across the free ends of the wire.

Thermostatic Expansion Valve

An automatic variable device controlling the flow of liquid refrigerant.

TORR

A unit of measure equivalent to the amount of pressure in 1000 microns.

Transition Glass Temperature

The glass-transition temperature (T_g) of a material characterizes the range of temperatures over which glass transition occurs. It is always lower than the melting temperature, (T_m) of the crystalline state of the material, if one exists. The glass-liquid transition or glass transition for short is the reversible transition in amorphous materials (or in amorphous regions within semicrystalline materials) from a hard and relatively brittle "glassy" state into a molten or rubber-like state, as the temperature is increased. An amorphous solid that exhibits a glass transition is called a glass.

Unloading Valve

This valve connects the interstage with suction to equalize both pressures during pump-down.

Virtual leak

In the vacuum system a virtual leak is the passage of gas into the chamber from a source that is located internally in the chamber.