Life Sciences

INDUSTRY

- **Control and sequencing**
- **Recipes**
- **Batch control and reporting**
- **Setpoint programming**
- **Bespoke displays**
- **Alarm management**
- **21 CFR Part 11**

The Freeze Drying Process

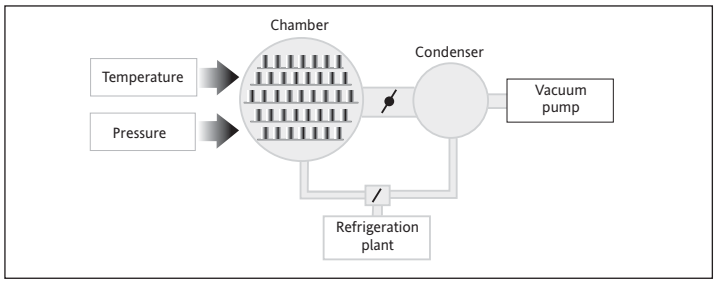
Application Note

Freeze drying is a slow batch process used in pharmaceutical and biochemical industries to extract dry product from an aqueous solution. The product is usually in phials placed on shelves in a vacuum chamber, which is first frozen and then evacuated. The shelves are then warmed up very slowly, boiling off the liquid, whilst the chamber is continuously evacuated through a cold condenser. Once above zero degrees the chamber isolation valve is closed and a 'Pressure Rise Test' is performed to ensure the product is dry.

Because of the high value of the product even automated freeze dryers go to wait states where the operator validates the readiness of the process to move on to the next stage.

Design and control

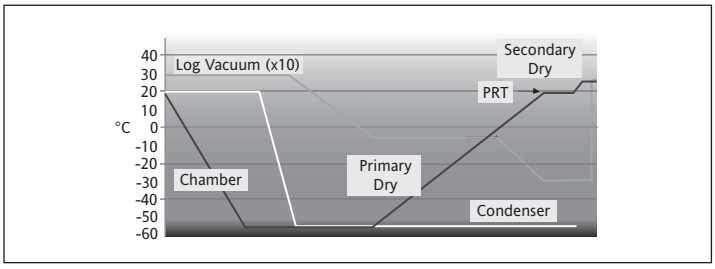
There are many different arrangements for freeze dryers but the basics are outlined here.



Temperature can either be controlled electrically using heating mats on the shelves, or by circulating oil through pipes welded to the shelves in the chamber. The temperature of the chamber, shelves (and/or heating oil), plus condenser form part of the control and monitoring variables.

The vacuum pressure is measured with a Pirani gauge. Control is achieved either by an analogue needle valve or coarse and fine admittance valves. A changeover valve is used to switch the refrigeration plant from freezing the chamber to freezing the condenser. In the final drying stage, the condenser, by then full of ice, may be isolated.

The freeze drying process is characterised by long stabilisation periods, for example when the chamber is first frozen, to ensure all the product is completely frozen before the chamber evacuation starts. This is a typical situation where the operator may be required to visually check and confirm that the product and plant are ready for the evacuation to proceed.



The critical phase is the heating phase where the rate at which the water boils off must be slow enough not to damage the product. During this phase, the vacuum is held constant to give consistent conditions. The temperature ramp has to be held if the vacuum rises too much, indicating that the water is coming off too fast.

At the end of the Primary Drying heat ramp, a Pressure Rise Test (PRT) is performed. Here the chamber isolation valve is closed for a defined period - if the product is dry the vacuum is maintained, if the pressure rises more than a nominal amount the product is not completely dry. In this case, the isolation valve is then reopened for another period before a second test is performed.

After the PRT, Secondary Drying takes place to ensure absolute dryness. The product is brought up to or just above ambient temperature.

The plant usually requires sterilisation. This is achieved by an alternative strategy within the control system.

A control system must therefore provide excellent HMI and flexibility, in addition to accurate and reliable control of each freeze drying cycle. It will include the following features:

- Precise temperature control with ramping
- Sequential control of the temperature, vacuum and the refrigeration plant, both for freeze drying and sterilisation
- Safety strategies to ensure product is not damaged as a result of plant failure
- Clear indications to the local operator of key process parameters and states
- Collection of data for analysis and evidence

Eurotherm® Eycon™ Visual Supervisor

The Eurotherm® visual supervisor is ideal for autoclave applications because it combines all these key features into a single compact unit:

- **Powerful loop and sequence control**
- **Flexible graphics**
- **Setpoint programmer**
- **Batch control and reporting**
- **Audit trail**
- **XGA touchscreen display to IP65**
- **Secure data logging and trending**
- **Recipe management**
- **Alarm management**
- **Access control and electronic signatures**

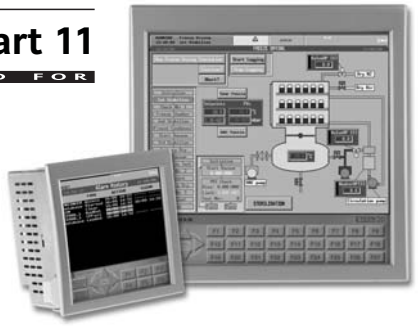
21 CFR Part 11 - 'Ready to use!'

Freeze drying plants are used in industries likely to require validation to the requirements of the FDA, EMEA or other applicable regulatory body. The visual supervisor has been widely used in validated processes including freeze dryers, autoclaves, reactors, fermenters, purified water systems, tablet coating machines, etc.

The Auditor feature on the visual supervisor has been specifically designed to meet the requirement of the FDA's 21 CFR Part 11 including:

- Controlled user access
- Secure data logging in tamper resistant format
- Audit trail recording user actions and changes to process parameters
- Electronic signature

21 CFR Part 11
ENHANCED FOR



With the Auditor feature, Electronic signature is configurable for all actions which may be performed from the visual supervisor display including the customised display and standard features such as batch, recipe changes, access control changes, etc.

Scalable architecture

A complete system can be created in combination with T2550 DIN rail I/O bases. Connection is via ELIN and I/O is scalable by adding 4. 8 or 16 slot bases as required. A range of I/O modules caters for the various interfaces required:

Analogue inputs	Freeze dryer temperature and pressure, condenser temperature, pumps RPM
Analogue outputs	Water, steam and nitrogen control, control valves, heater, vacuum retransmission
Digital inputs	Valve limit switches, pump status
Digital outputs	Valve control solenoids, vacuum and circulation pump controls

System building blocks:

- Single freeze dryer (single Eycon™ visual supervisor)
- Multiple units with supervisory workstation(s)

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