

Gentle Drying Process and a Longer Shelf Life

Sensor and measurement technology for freeze dryers in accordance with FDA requirements

Freeze-drying is used in the manufacture of pharmaceutical products to ensure that they have a longer shelf life. The measurement technology used in this process must be reliable, deliver accurate results, and be securely documented.

Freeze-drying is a process in which products are gently dried. This process is often used for valuable products, such as antibiotics, that cannot be stored for long periods of time when they are aqueous. Other drying procedures are rarely used for these products, if at all. The high temperatures that are used in spray drying or drum drying could damage these products or irreversibly change them. As a result, highly sensitive products are dried using a freeze-drying process.

Freeze-drying process

A freeze-drying unit consists of two chambers that are connected to one another and can be locked with a valve. The product that needs to be dried is first placed on a tray that can be heated and cooled and is first deep-frozen at a standard pressure. A capacitor is installed in the second chamber through which refrigerant flows. In the next step, a vacuum is generated which sublimates the water that is contained within the product. The principle underlying this process is that even in its frozen form, water still contains a sufficient level of vapor pressure to turn straight from a frozen to a gaseous state. During this sublimation, energy is absorbed.

Because thermal energy is drawn from the ambient temperature, the temperature in the drying chamber may drop during the process. To maintain a constant temperature, the chamber is supplied with the same amount of heat that is absorbed by the water as sublimation energy. The next stage of the process is secondary drying, where bound water is removed from the product through additional warming.

To cool the product, either a coolant (for example silicone oil) is used, or refrigerant is applied directly (usually nitrogen or carbon dioxide). The temperatures of the capacitor are typically -60 to -80 °C.

Limit values must be specified for each process variable to which the product may be subjected during freeze-drying. If there is a one-off or repeated effect on the physical and chemical properties of the product, the worst case scenario must be assumed for every combination of process parameters. Examples of some of the process variables include:

temperature and pressure, speed of the temperature and pressure change, and dwell time at the relevant extreme values.

JUMO has developed sensors especially for the cyclical operating conditions prevalent in freeze-drying and has experienced a lot of success in this sector for a number of years.

Temperature measurement

The special design of push-in RTD temperature probes enables them to be used in steamy, pressurized atmospheres with the protection type IP 69. The PTFE connecting cable is designed for use in humid environments in a temperature range from -190 to +260 °C. The connecting cable transition point to the thermometer is strain-relieved. A Pt100 temperature sensor is used in a two-wire circuit as a standard measuring insert according to DIN EN 60 751, class A. Redundant versions with two or three measuring circuits are also available. The sensors can also be connected in a three- or four-wire circuit, depending on requirements.

Pressure measurement

Depending on the application, different pressure transmitters are used. For production facilities that manufacture pharmaceuticals, the JUMO dTRANS p31 pressure transmitter is used in two- or three-wire variants to measure liquid and gas media. The nominal measuring ranges span 0 to 25 bar absolute pressure and -1 to 0 bar up to a maximum of 0 to 60 bar relative pressure. In principle, the range of process connections allows the user to choose between a welded, sealless system or a screwed, sealed system. The process connection must be free of dead space and easy to clean. For this purpose, a process connection adapter with modular construction is available that is especially designed with the demands of hygienic process reliability in mind. It is worth highlighting the high temperature measuring cell, which permits consistently high and strongly fluctuating medium temperatures from -30 to +200 °C.

The JUMO MIDAS S05 is the ideal product for laboratory facilities. This pressure transmitter is also available with relative pressure or absolute pressure measuring ranges. The fully welded measuring system (without

seals) made of high-quality stainless steel allows this device to be used in almost all media, even in harsh conditions. The silicon sensor has an extremely high overload capacity and can cope with several million pressure cycles.

Recording

During freeze-drying, it is essential that the measuring devices respond quickly and work accurately and reliably. A JUMO LOGOSCREEN can check and document the process progress here. This paperless recorder graphically displays the measured values during the process whilst simultaneously documenting and archiving the information in a forgery-proof manner. The device fulfils the requirements of the FDA 21 CFR Part 11 in particular and is therefore ideal for documenting pharmaceutical processes such as freeze-drying. The batch reporting and Web server functions represent additional benefits of the device. Up to three batch reports can be created simultaneously in the paperless recorder. The measuring data, the start, end, and duration of every batch can be displayed on the paperless recorder and in the PC Evaluation Software, together with a batch number and freely definable text. On request, the batches can be started using a bar code reader and the batch text can be read in. The Web server is integrated into the paperless recorder as standard. This can be used to create four different types of display, such as online visualization, three freely programmable HTML pages, current batch reports, and a 4-way view (1 to 4 recorders or different visualizations). The Web server can be accessed via a PC using Microsoft® Internet Explorer. With the new software version 187.04.01 and later, the LOGOSCREEN fd supports a total of 54 external channels (both analog and digital), which can be used via a Modbus interface (master/slave), PROFIBUS interface, and Ethernet (Modbus TCP slave). In addition, it is now possible to switch the recorder display from portrait to landscape, depending on which view the customer prefers.

Summary

The basic principle of freeze-drying is to give highly sensitive products a longer shelf life. This is achieved through processing with the aid of temperature, pressure, and time. These factors are dependent on each other and work together to determine the best possible outcome. JUMO offers fast-response, steam-proof sensors and reliable measuring and recording technology to securely control and monitor freeze-drying processes.