Special care is taken during process development to ensure that the crystalline form, size range, moisture content, etc. are optimal to help the powder flow freely during the powder-filling step. Unimpeded powder flow is essential to do aseptic powder fill operation. The sterile powder is collected in aluminum containers, and ported to sterile powder-filling machines, and filled in de-pyrogenated/presterilized vials to obtain the finished product, described further below.

Vacuum-Drying

Although less often used than freeze-drying, vacuum-drying has found its use in making pharmaceutical products. As the name suggests, the process does not entail freezing, but application of vacuum only, at low temperatures. Typically the drug is dissolved in ethanol, loaded on to freeze-dryers, the shelf temperature brought down to −25 to −35 °C, and a vacuum is applied. Care is taken to ensure that the contents of the vial does not "boil" at the low pressure, as this will likely lead to the contents being expelled from the vial. At the end of the cycle, the vials will be left with the active drug in the form of a film. Often the film is barely visible—depending upon the quantity of active used. Sometimes, an excipient soluble in ethanol is added to the formulation, so that the finished product does appear to be a visible film, amenable to easier visual inspection.

In cases in which a lower vapor pressure solvent is required to achieve dissolution of the API, a cosolvent approach can be taken to increase the vapor pressure to make the formulation amenable to vacuum-drying [6]. Examples of such solvents are dimethyl acetamide and dimethyl sulfoxide.

Vacuum-drying cycles are easier to develop than standard freeze-drying cycles. There is no need to determine a collapse temperature or eutectic point. Formulation development is significantly reduced, as the only requirement to be met is that the active be soluble in ethanol and that there is no alcohol—drug chemical reaction. The one critical parameter to observe is the potential for the contents of the vial to boil over. Typically, vacuum-drying cycles are shorter when compared with freeze-drying. In view of the flammability of ethanol, explosion-proof equipment will be necessary. Typically, this can add significant cost for capital equipment, and may explain why vacuum-drying is not more widely used.

The process for manufacturing vacuum-dried products is not significantly different from that used for regular freeze-drying. The active is dissolved in ethanol (sometimes an excipient is added for enhancing visual appearance), sterile filtered into pre-cleaned and de-pyrogenated vials, and loaded on to freeze-dryers. Shelf temperature is lowered to −25 to −35 °C, and vacuum is applied. Prior laboratory work will have been done to select the optimal vacuum and shelf temperature, in order to ensure that the contents do not boil over.

Commercially available pharmaceutical products which avail vacuum-drying technology include the cytotoxic drugs carmustine and lomustine.