EQUIPMENT

In some instances a product may be frozen in a bulk container or in trays rather than in the final container and then handled as a bulk solid. Such a state requires a continuation of aseptic processing conditions as long as the product is exposed to the environment.

When large quantities of material are processed, it may be desirable to use ejection pumps in the equipment system. These draw the vapor into the pump and eject it to the outside, thereby eliminating the need for a condensing surface. Such pumps are expensive and usually practical only in large installations.

Available freeze-dryers (suppliers: BOC Edwards, FTS, Hull, Serail, Stokes, Usifroid, Virtis, others) range in size from small laboratory units to large industrial models. Their selection requires consideration of such factors as:

- The tray area required
- The volume of water to be removed
- How the chamber will be sterilized
- Whether internal stoppering is required
- Whether separate freezers will be used for initial freezing and condensation of the product
- The degree of automatic operation desired

Other factors involved in the selection and use of freeze-drying equipment are beyond the scope of this chapter, but references (2,3), and (5) can be consulted for more information as well as, of course, technical discussions with freeze-drying equipment manufacturers.

Freeze-drying is being used now for research in the preservation of human tissue and is finding increasing application in the food industry. Most biopharmaceuticals require lyophilization to stabilize their protein content effectively. Therefore, many newer developments in the lyophilization process focus on the requirements of this new class of drug products.

Aseptic Technologies (Gembloux, Belgium) has introduced the concept of "closed-vial" technology (discussed in chap. 23) and this includes the ability to freeze-dry vials (44). Vials are stoppered prior to filling with filling occurring through a needle piercing the rubber closure. The needle gauge for filling of vials for freeze-drying is 11G, slightly larger than the 13G used for vials that are not freeze-dried. A device called a "penetrator" is placed on top of the vial, then the vial, still closed, is conveyed to the freeze-dryer shelf. Once all vials are located within the freeze-dryer and the door closed, the shelves are moved downward, pushing on the penetrator's cone that reopens the piercing trace made by the 11-G filling needle. The lyophilization cycle is started with the shelves kept at the low position to keep the stoppers open via the penetrator. At the conclusion of the cycle, the shelves are lifted, the stopper assumes its original shape, the penetrator is lifted, and the rubber stopper re-seals. Vials are removed from the dryers, penetrators removed, and laser re-sealing of the stopper occurs (see chap. 23 for further explanation). At the time of this publication, the author was not aware of any company adopting this technology, but perhaps it is only a matter of time before such technology becomes state-of-the-art. There are still many challenges and limitations with the closed vial concept, as will be discussed in chapter 23.

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