sterilization is very slow because heat transfer occurs by convection in air, a poor heat conductor. Heat penetration is slower than steam heat because of the long exposure times required to kill resistant spore organisms. The high temperatures required may cause degradation of materials, this being a major limitation of the wide applicability of dry heat as a sterilization method. Heat penetration through steel is faster than penetration through glass. Heat must penetrate to interior surfaces of items via conduction. Reflectance from shiny surfaces and differences in air density with temperature will have significant effects on the rate and extent dry heat sterilization. Of course, air tends to stratify, so fans or blowers must be used to aid heat circulation. One final limitation—materials will expand during heating and contract during cooling. Contraction could draw in microorganisms; therefore, all openings must be covered securely.

Dry heat sterilization is accomplished using either cabinet ovens or conveyer tunnels. With cabinet ovens, filtered air flows across the load, moved by a blower. High efficiency particulate air (HEPA) vent filters are used for the air inlets and outlets. There is always a concern about particulate matter being generated from the heat source. The door opening to the dryer must be sealed adequately. Temperature, time, and blower speed are controlled. The size of the chamber is limited, and manual loading and unloading are required that limit the rate of processing.

Tunnel sterilizers are conveyor systems where primarily glass containers are sterilized and depyrogenated while moving from a heat zone through a cooling zone. A schematic example of a dry heat sterilization and depyrogenation tunnel is shown in Figure 17-7. The source of heat is either convection or radiant heat while the cooling zone contains HEPA-filtered, vertical laminar air flow units. The conveyor belt is stainless steel and containers are moved from a nonsterile area after washing to critical work area where they exist typically right onto a collection/accumulation table for immediate filling of sterile product. Tunnel dry heat sterilizers are used for products having large volumes of glass containers to be filled. Tunnel sterilizers are more difficult to validate (than cabinet ovens) are more difficult to control uniform heating throughout the conveyor system, and, like any dry heat system, may generate particles from the heating zone.

Gas Sterilization

Many gases have been tried and used over the years to sterilize pharmaceutical materials. Most prominent of these gases have been ethylene oxide, peracetic acid, chlorine dioxide, and vapor phase hydrogen peroxide. Other gases used less frequently or not at all any more include formaldehyde, propylene oxide, beta propiolactone, and ozone. Items traditionally sterilized by gases include plastic containers, gowning materials, plastic devices, and other heat-labile equipment and materials.

Ethylene oxide (EtO) (Fig. 17-8) has been the classic sterilization gas. It is an alkylating agent that is very potent and highly penetrating. It is also a carcinogen. For many years it was used in a mixture with Freon, normally 12 parts EtO and 88 parts Freon. When the use of Freon was banned in 1996, EtO had to be used either as 100% (relatively dangerous because of its flammability) or in combination with carbon dioxide.

EtO lethality is influenced by four main factors:

1. Gas concentration—Ranges used are 400 to 1200 mg/L
2. Temperature—Temperature used depends on gas concentration used. Normal temperature range is 50°C to 60°C
3. Relative humidity—The normal range used is 35% to 80% RH. The *D* value of biological indicators used for EtO sterilization validation may range up to 10-fold over the range of RH values
4. Exposure time.

One of the major drawbacks of using EtO as a sterilization gas is its reacting with water or other components of the item(s) being sterilized and forming EtO residual compounds. These residual compounds at certain levels are hazardous to people and to the environment. For years, there have been threats both by the occupational safety and health organization (OSHA) and the environmental protection agency (EPA) to ban the use of EtO because of residuals. Typical EtO residuals are ethylene glycol from the reaction of EtO and water, and ethylene chlorhydrin from the interaction of EtO and chloride compounds. Each residual level has an upper limit that is usually achievable through aeration of the material after EtO exposure.