Table 17-6 ISO 10933-7 Requirements for Ethylene Oxide Residuals

Exposure	Patient exposure	Average daily dose to patient	Dose in first 24 hours	Dose in first 30 days	Dose over lifetime
Limited	Contact up to 24 hours	EtO < 20 mg ECH < 12 mg ECH < 12 mg	EtO < 20 mg ECH < 12 mg ECH < 12 mg	Not applicable	Not applicable
Prolonged	24 hours to 30 days	EtO < 20 mg ECH < 12 mg	EtO < 2 mg/day ECH < 2 mg/day	EtO < 60 mg ECH < 60 mg	Not applicable
Permanent	Greater than 30 days	EtO < 20 mg ECH < 12 mg	EtO < 0.1 mg/day ECH < 2 mg/day	EtO < 60 mg ECH < 60 mg	EtO < 2.5 mg ECH < 50 mg

The International Organization for Standardization (ISO) developed ISO10993-7 entitled "Biological Evaluation for Medical Devices—Part 7: Ethylene Oxide (EtO) Sterilization Residuals" (1995) that specified requirements for establishing allowable limits of EtO residuals on medical devices (Table 17-6). Formerly, the FDA in 1978 established limits as:

Ethylene oxide	250 ppm
Ethylene chlorhydrin	250 ppm
Ethylene glycol	500 ppm

A typical EtO sterilization cycle is shown in Figure 17-9. Note that the sterilization exposure period is relatively long and, although not shown, the aeration period also can be very long, up to 24 hours or more.

Chlorine dioxide and vapor phase hydrogen peroxide (VPHP) are alternative gas sterilization agents, both used primarily to sterilize surfaces of flexible and rigid barrier isolation systems. Ozone and peracetic acid are other alternative agents with some applications in the parenteral industry, ozone for deionized water treatment, peracetic acid for isolator sterilization. Chlorine dioxide typically uses a mixture of 2% chlorine gas and 98% nitrogen, and employs cycle parameters (vacuum, humidity, gas exposure time, aeration time) similar to EtO cycles although chloride dioxide sterilization cycles are shorter. Penetration of materials is better with chloride dioxide that with VPHP, but neither gas can penetrate as readily as EtO. Chlorine dioxide gas has a greenish color that is easily seen during a sterilization cycle.

VPHP has been the standard sterilant of choice for isolators. It is a very effective sporicidal agent, relatively safe, and environmentally friendly. The vapor form of peroxide, unlike the

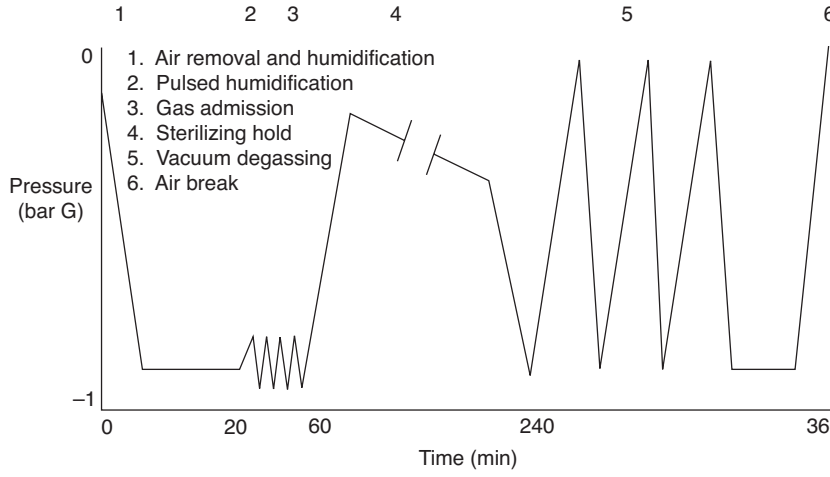

Figure 17-9 Schematic diagram of a 100% ethylene oxide sterilization cycle. *Source*: From Ref. 10.