with scale-up. Consider the probability of an unsuccessful fermentation, $[1 - P_0(t)]$, in a reactor,

$$1 - P_0(t) = 1 - \left[1 - p(t)\right]^{N_0} \tag{10.19a}$$

or with a simple model of killing in homogeneous populations:

$$1 - P_0(t) = 1 - \left[1 - e^{-k_d t}\right]^{N_0} \tag{10.19b}$$

N_0 in eq. 10.19 corresponds to the number of individuals in the reactor, not the concentration of organisms. Let n_0 be the concentration of particles. Now consider the probability of an unsuccessful sterilization in a 1 l and 10,000 l reactor, where each contains the same identical solution (n_0 is the same in both tanks), and the temperature (k_d) and time of sterilization are identical. Thus, for the 1-l tank

$$1 - P_0(t) = 1 - \left[1 - e^{-k_d t}\right]^{1 \cdot n_0} \tag{10.20a}$$

and for the 10,000-l tank

$$1 - P_0(t) = 1 - \left[1 - e^{-k_d t}\right]^{10{,}000 \cdot n_0} \tag{10.20b}$$

If $k_d t$ is 15 and $n_0 = 10^4$ spores/l in both cases, the probability of an unsuccessful fermentation is 0.003 in the 1-l vessel and about 1 in the 10,000-l tank ($5 \cdot 10^{-14}$ probability of extinction of the spores). Thus, the sterilization protocol that would be acceptable for a laboratory bench-scale experiment would be totally unacceptable for the larger-scale system. The larger tank would require much longer exposure to the same temperature to achieve the same degree of sterility, and the longer exposure to higher temperatures could lead to greater changes in the chemical composition of the medium.

A *sterilization chart* can be constructed from eq. 10.19b. An example is depicted in Fig. 10.14. To use such a chart, you need to specify the probability of failure that is acceptable (for example, 10^{-3}) and the number of particles initially present in the fluid ($n_0 \cdot$ total volume). For 10^{-3} and $N_0 = 10^8$, the corresponding value of $k_d t$ is about 26. If $k_d = 1$ min^{-1} at 121°C, then $t = 26$ min corresponds to the exposure time at 121°C required to ensure that 999 sterilizations out of a 1000 are successful.

Steam sterilizations can be accomplished batchwise, often *in situ* in the fermentation vessel, or in a continuous apparatus (Fig. 10.15). The greatest difficulty with batch sterilization is thermal lags and incomplete mixing. Typically, batch sterilization occurs at 121°C. The time required to heat the fluid to 121°C and to cool it back to growth temperatures (e.g., 37°C) is often much longer than the time of exposure to the desired temperature. For most spores, k_d falls very rapidly with temperatures (e.g., a tenfold decrease for k_d at $T = 110$°C rather than 121°C), so the heat-up and cool-down periods do little to augment spore killing. However, the elevated temperatures during heat-up and cool-down can be very damaging to vitamins and proteins, can lead to carmelization reactions for sugars, and can greatly alter medium quality.

Continuous sterilization, particularly a high-temperature, short-exposure time, can achieve complete sterilization with much less damage to the medium. Both the heat-up