Table 13-1B Common Sporocidal Agents Used for Contamination Control in Parenteral Manufacturing Facilities

	Advantages	Disadvantages
Sodium hypochlorite (Bleach) (typically 5% solution)	Very rapid activity, especially freshly prepared and buffered to pH 7.6	Organic matter reduces effectiveness
Vaporized hydrogen peroxide	Excellent activity	Prone to decomposition
Glutaraldehyde	Excellent activity Superior to formaldehyde	Less effective at acid pH
Iodophors	Depends on availability and concentration of iodine	Less potent than glutaraldehydes Activity less at alkaline pH

Source: From Ref. 9.

The United States Pharmacopeia (USP) contains a chapter <1072> entitled "Disinfectants and Antiseptics" that addresses subjects such as:

- Selecting chemical disinfectants and antiseptics
- Demonstrating the effectiveness of disinfectants as bactericidal, fungicidal, or sporicidal agents
- Applying disinfectants in manufacturing areas.

Choices of sanitizing agents must be validated for their effectiveness. Validation primarily involves reproducible bactericidal (or sporicidal) activity of the sanitizing agent. Manufacturers differ with respect to frequency of revalidation after initial validation, with some of them doing no revalidation and others revalidating on an annual basis. Microorganisms used in validation are typically environmental isolates. A 2 to 3-log reduction in inoculum challenge is required. Validation is performed using membrane filters or surface testing. Some manufacturers use polysorbate 80 solutions to neutralize surfaces during validation.

Organic materials inactivate most sanitizing agents. Sanitizing effectiveness depends on such factors as time exposure, concentration of agent, pH, hydration, and temperature. The physical removal when using sanitizing agents on hard surfaces is as much or possibly more important as chemical destruction.

The largest use of sanitizing agents is for decontaminating floors where most floors are sanitized (mopped) at least daily, perhaps multiple times a day. Walls are sanitized less frequently than floors. Equipment surfaces, workstations, chairs, communication systems, and other surfaces that cannot be sterilized are sanitized regularly. Sanitization can be classified as

- "Deep-cleaning"—generally done after an area shutdown
- Routine—daily or some other frequency during normal operations
- Continuous—for example, frequent sanitization of gloved hands and utensils used during manufacturing.

It has become standard practice that disinfectants should be rotated with sufficient frequency to avoid the development of resistant strains of microorganisms (10). The European Commission's Good Manufacturing Practice Guidelines on the Manufacture of Sterile Medicinal Products advocates disinfectant rotation while the FDA's Aseptic Processing Guidelines do not. Most sterile product manufacturers rotate sanitizing agents either on a weekly or monthly basis. However, in reality, there is no need to rotate disinfectants unless there are data from environmental monitoring samples that suggest rotation must be implemented. Data that suggest rotation is needed would include

- A trend in breaches in alert/action levels in the EM program
- Recovery of repetitive isolates subsequently shown not to be inactivated by the disinfectant.

The material used to apply sanitizing solutions to surfaces must not only hold a certain amount of solution, but, as importantly, must also deposit the solution readily and evenly on the surface. A variety of fabric wipers are available, but the most common type are wipers