Some manufacturers have incorporate antimicrobial preservative agents in the formulation to aid in the sterilization of marginal sterilization practices like tyndallization, but again, these practices today are unacceptable from a sterilization validation standpoint.

Articles to be sterilized must be properly wrapped or placed in suitable containers to permit penetration of sterilants and provide protection from contamination after sterilization. Sheets or bags made of special steam-penetrating paper or polymeric materials are available for this purpose. Further, containers or bags impervious to steam can be equipped with a microbe-excluding vent filter to permit adequate steam penetration and air exit. Multiple wrapping permits sequential removal of outer layers, as articles are transferred from zones of lower to higher environmental quality. The openings of equipment subjected to dry heat sterilization often are covered with metal or glass covers. Laboratories often used silver-aluminum foil for covering glassware to be used for endotoxin testing. Wrapping materials commonly used for steam sterilization may be combustible or otherwise become degraded under dry heat sterilization conditions.

The effectiveness of any sterilization technique must be proved (validated) before it is employed in practice. Since the goal of sterilization is to kill microorganisms, the ideal indicator to prove the effectiveness of the process is a resistant form of an appropriate microorganism, normally resistant spores (a biological indicator, or BI). Therefore, during validation of a sterilization process, BIs of known resistance and numbers are used in association with physical-parameter indicators, such as recording thermocouples. Once the lethality of the process is established in association with the physical measurements, the physical measurements can be used for subsequent monitoring of in-use processes without the BIs. Eliminating the use of BIs in direct association with human-use products is appropriate because of the ever-present risk of an undetected, inadvertent contamination of a product or the environment. The number of spores and their resistance in BIs used for validation studies must be accurately known or determined. Additionally, the manner in which BIs are used in validation is critical and must be controlled carefully.

In addition to the data printout from thermocouples, sometimes other physical indicators are used, such as color change and melting indicators, to give visual indication that a package or truckload has been subjected to a sterilization process. Such evidence can become a part of the batch record to confirm that sterilization was accomplished.

Table 17-7 provides a comprehensive listing of all the ISO standard documents for sterilization of health care products.

PARAMETRIC RELEASE

Many products, especially large-volume injectables, that are terminally sterilized using overkill cycles, can be released to the market without the need to perform compendial sterility testing. Parametric release must be approved by the FDA or other appropriate regulatory body. Parametric release requires well-defined and validated sterilization cycles where the physical parameters of processing are well defined, predictable, measurable, and the lethality of the cycle has been microbiologically validated (4). Both FDA and EU guidelines permit parametric release of products with prior approval (5,6).

Sterilization Information Required for Commercialization of Sterile Products

The FDA published a guidance document that is still used today for submitting documentation related to the sterilization and validation of that sterilization process for a sterile drug product (7). Any new or abbreviated drug application for marketing of a sterile drug product must submit documentation that clearly details how the product is rendered sterile and sterility maintained from preparation, through release and throughout the shelf-life period of every batch of the product. Table 17-8 summarizes what is contained in this guidance document.

REFERENCES

1. Shirtz J. F, D and z values. In: Agalloco JP, Carleton FJ, eds. Validation of Pharmaceutical Processes. 3rd ed. Informa, New York: CRC Press, 2007:159–173.
2. Pflug IJ. Heat sterilization. In: Phillips GB, Miller WS, eds. Industrial Sterilization. Durham, NC: Duke University Press, 1973:239–282.