Part 11 requirements have been expected, but at the time of this publication, still have not been published.

FACILITIES AND EQUIPMENT PREPARATION

Sterile product facilities need to be constructed of materials that are smooth, cleanable, and resistant to physical and chemical deterioration. Elaboration of facility construction, requirements, and controls are presented in chapter 14.

There are a significant number of equipment items that are involved in sterile product manufacturing. Examples of typical equipment items used in sterile product manufacturing are listed in Table 12-3. For each of these types of equipment, accurate documentation much be maintained that includes maintenance, cleaning, sterilization, and usage. Advances in manufacturing equipment must be monitored by appropriate personnel so that state-of-the-art equipment is used, particularly to enhance quality of the resulting product.

GENERAL MANUFACTURING PROCESS

The preparation of a parenteral product includes procurement of all components, applying all appropriate manufacturing process to compound, mix, fill, and close the unit dosage form, packing and labeling of the dosage forms, and controlling the quality of the product at all steps of the process. The general flow of the manufacturing process along with the environmental quality of each step of the process is given in Figure 12-2.

Procurement encompasses selecting and testing according to specifications of the raw-material ingredients and the containers and closures for the primary and secondary packages. Microbiological purity, in the form of bioburden and endotoxin levels, have become standard requirements for raw materials. Raw material providers need to be audited by sterile product manufacturers using their products. It is acceptable for sterile product manufacturers to accept raw material certificates of analysis without the need to repeat any specification tests except for an identity test upon receipt of the material.

Processing includes cleaning containers and equipment to validated specifications, compounding the solution (or other dosage form), filtering the solution, sanitizing or sterilizing the containers and equipment, filling measured quantities of product into the sterile containers, stoppering (either completely or partially for products to be freeze-dried), freeze-drying, terminal sterilization if possible, and final sealing of the final primary container.

Table 12-3 List of Production Equipment for Production of Sterile Products

- Washing equipment for packaging components
  - Glass container washer
  - Rubber closure washer (plus siliconizer, depyrogenator, sterilizer)
  - Plastic tubing washer
- Mixing tanks
- Laminar air flow units with HEPA filters
- Dry heat ovens and tunnel sterilizers
- Steam sterilizers
- Clean-in-place and steam-in-place systems for large equipment
- Filter equipment—liquid and gas
- Storage tanks
- Filling equipment—ampoules, vials, syringes, cartridges, bags, bottles
- Stoppering equipment
- Sealing equipment
- Freeze-dryers
- Barrier isolators
- Packaging and labeling equipment
- Particle detectors
- Environmental monitoring systems
- Homogenizers/mills/micronizers