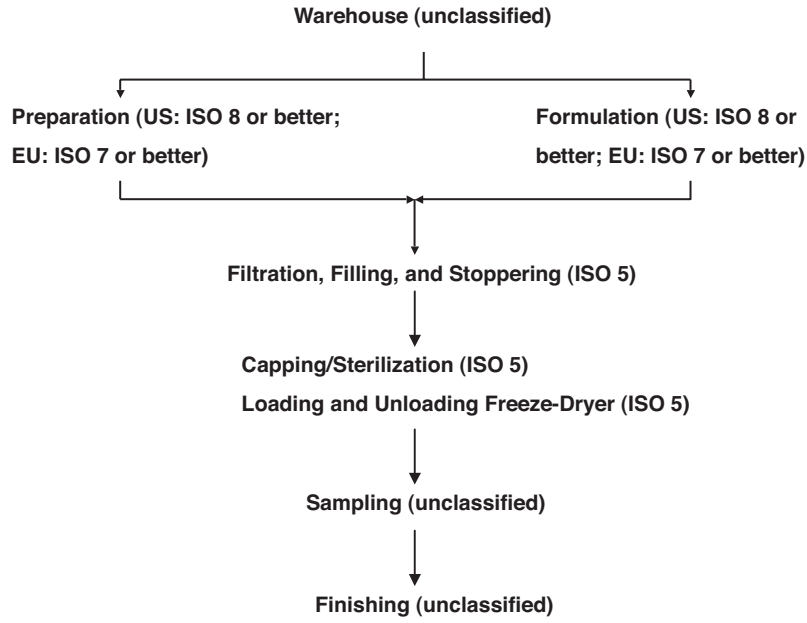

Figure 12-2 Flow of sterile manufacturing (Air classification of each area).

Packaging normally consists of the labeled, cartoned, filled, and sealed primary containers. The control of quality begins with the incoming supplies, being sure that specifications are met. Careful control of labels is vitally important as errors in labeling can be dangerous for the consumer. Each step of the process involves checks and tests to be sure that the required specifications at the respective step are being met. Labeling and final packaging operations are becoming more automated.

The quality control unit is responsible for reviewing the batch history and performing the release testing required to clear the product for shipment to users. A common FDA citation for potential violation of cGMP is the lack of oversight by the quality control unit in batch testing and review and approval of results.

PRODUCT PREPARATION

Preparation of Components

Components of sterile products include the active ingredient, formulation additives, vehicle(s), and the primary container and closure. Establishing specifications to ensure the quality of each of these components is essential. For sterile preparations, two of the most critical specifications are microbial and endotoxin levels in each raw material. All cleaning operations for all components must be validated that the cleaning processes remove all extraneous chemical material and particulate matter. Cleaning validation of equipment is subject of many publications, seminars, and regulatory documents and had not been covered in this book other than to indicate it.

The most stringent chemical-purity requirements normally will be encountered with aqueous solutions, particularly if the product is to be sterilized at an elevated temperature where reaction rates will be accelerated greatly. Dry preparations pose relatively few reaction problems but may require definitive physical specifications for ingredients that must have certain solution or dispersion characteristics when a vehicle is added.

Compounding (or Formulation)

Compounding is the preparation of the product to be filled into the primary container. Facility classification for compounding typically is Grade D (ISO 8) or better. The development of the