The control strategy for the filling operation involves confirmation of uniformity, and for peptide or protein-based preparations measurement can be achieved by nitrogen determination, colorimetric test, or an HPLC assay. A statistically defined set of samples across the entire filling operation of the batch is typically evaluated due to the destructive nature of testing. Continuous on-line measurement of optical density is also a possibility, and offers the advantage of nondestructively examining every container for appropriate uniformity. However, process analytical technology (PAT) approaches require development, validation and maintenance of measurement equipment, and associated computer models.

Control Strategy

Final batch release testing to confirm quality consists of a set of attributes, test methods, and acceptance criteria that comprise the product specification. However, it is important to appreciate that the batch specification only represents one part of the overall control strategy. There are a number of required tests for sterile injectable products including assays for identity, content, purity, extractable volume, sterility, and endotoxin that must be included before product can be released to the market. Any additional testing that is included at this point depends on the design of the overall control strategy. Many options for implementing various control elements throughout a suspension process have been highlighted in the text of this section so there may not be a need to repeat certain tests at batch release. For suspension products, it might be appropriate to include in the specification measurement of particle morphology, particle size and distribution, or rheological properties depending on the nature of the final suspension. Multiuse suspension products containing a preservative may include a content determination for this excipient to ensure that the concentration remains in the range effective for antimicrobial effectiveness. Finally, this discussion only considered a subset of the unit operations involved in suspension manufacture and does not represent a complete description of a suitable control strategy for a pharmaceutical product.

Additional coverage of suspension manufacture is found in chapter 12.

EMULSIONS

Emulsions for injection exist both as large-volume and small-volume products. Injectable emulsions are oil in water systems with the oil phase as the internal or dispersed phase and the water phase as the external or continuous phase. Globule size for emulsions range from 0.1 to 50 μm with emulsions administered by intravenous injection or infusion needing to be of globule size less than 1 μm. Large-volume emulsions are used for parenteral nutrition purposes while small-volume emulsions are considered alternative dosage forms for poorly water-soluble drugs.

Large-volume fatty lipid emulsions are used in parenteral nutrition therapy. Formulations are typically as follows:

Soybean oil	10–20%
Egg yolk phospholipid	1.2%
Glycerin	2.5%
Water	QS

Large-volume emulsions have a pH around 8 and are terminally sterilized using patented steam sterilization cycles that maintain the globule size distribution of the product so that it can be safely administered IV.

Small-volume emulsions for injection have the general formulation of the drug, soybean oil, egg lecithin, glycerin, and water. Drugs that are formulated into emulsion dosage forms include propofol, vitamins, dexamethasone, flurbiprofen, prostaglandin E1, diazepam, and perfluorocarbon.

It is very difficult to extemporaneously incorporate a water-insoluble drug into an existing emulsion formulation (e.g., large-volume emulsion) and have a stable product. The solubilization of the drug is marginal and the drug usually causes the emulsion to destabilize. Drug-containing emulsions should be prepared where the emulsion is formed after the drug is dissolved in the oil phase.