products of biotechnology where sometimes very small amounts of aggregated protein may be seen visually. While these aggregates are viewed as "particles," they are not viewed as "foreign material." Manufacturers differ on whether such containers with aggregated protein should be rejected. Some protein-containing products do allow for in-line filtration of the product prior to injection into the human body and the FDA permits this as long as the filtration does not filter out protein to the point that it fails potency specifications.

All large- and small-volume injections, unless otherwise specified in individual monographs, are subject to the particulate matter limits set forth under <788> Particulate Matter in Injections. Injections packaged and labeled for use as irrigating solutions are exempt from the requirements for Particulate Matter. Also, at the time of this writing, injections administered by the intramuscular or subcutaneous routes are exempted from the requirements for <788> although this will be changed in future USP editions (see Chap. 29).

Sterility

This section simply states that all preparations for injection must meet the requirements under Sterility Tests <71>.

Constituted Solutions

Dry solids are constituted at the time of use by health care practitioners. Therefore, tests and standards pertaining to the solution as constituted for injection are not included in the individual USP monographs for these products (also true for liquid concentrates). USP states that in the interest of assuring the quality of these preparations as they are actually administered, certain nondestructive tests are to be performed to demonstrate the suitability of constituted solutions prepared.

1. Completeness and Clarity of Solution—The product is reconstituted as directed in the labeling supplied by the manufacturer and observed for:
   a. The solid dissolves completely, leaving no visible residue as undissolved matter or
   b. the constituted solution is not significantly less clear than an equal volume of the diluent or of Purified Water contained in a similar vessel and examined similarly.
2. Particulate Matter—After the sterile dry solid is reconstituted according to the manufacturer's directions, the solution is essentially free from particles of foreign matter that can be observed on visual inspection.

REFERENCES

1. Guidance for Industry—Nonclinical studies for the safety evaluation of pharmaceutical excipients, United States Food and Drug Administration, May 2005. http://www.fda.gov/cber/guidelines.htm.
2. International Pharmaceutical Excipients Council of the Americas, Inc., Arlington, VA, 2010. http://www.ipecamericas.org/index.html.