to the requirements for *injectable suspensions* (e.g., Imipenem and Cilastatin for Injectable Suspension, USP)

The form in which the manufacturer prepares a given drug for parenteral use depends on the nature of the drug itself with respect to its physical and chemical characteristics and on certain therapeutic considerations. Generally, if a drug is unstable in solution, it may be prepared as a dry powder intended for reconstitution with a proper solvent at the time of administration, or it may be prepared as a suspension. If the drug is unstable in water, that solvent may be replaced in part or totally by a solvent in which the drug is insoluble. If the drug is insoluble in water, an injection may be prepared as an aqueous suspension or as a solution in a suitable nonaqueous solvent, such as a vegetable oil. If an aqueous solution is desired, a water-soluble salt form of the insoluble drug is frequently prepared. Aqueous or blood-miscible solutions may be injected directly into the blood stream. Blood-immiscible liquids, such as oleaginous injections and suspensions, can interrupt the normal flow of blood, and their use is generally restricted to other than IV administration. The onset and duration of action of a drug may be somewhat controlled by its chemical form, the physical state of the injection (solution or suspension), and the vehicle. Drugs that are very much soluble in body fluids generally have the most rapid absorption and onset of action. Thus, drugs in aqueous solution have a more rapid onset of action than do drugs in oleaginous solution. Drugs in aqueous suspension are also more rapid acting than drugs in oleaginous suspension because of the greater miscibility of the aqueous preparation with the body fluids after injection and the more rapid contact of the drug particles with the body fluids. Oftentimes, long action is desired to reduce the frequency of injections. These long-acting injections are called repository or depot preparations.

The solutions and suspensions of drugs intended for injection are prepared in the same general manner as solutions (Chapter 13) and disperse systems (Chapter 14), with the following differences:

1. Solvents or vehicles must meet special purity and other standards ensuring their safety by injection.
2. The use of added substances, such as buffers, stabilizers, and antimicrobial preservatives, falls under specific guidelines of use and is restricted in certain parenteral products. The use of coloring agents is strictly prohibited.
3. Parenteral products are always sterilized, must meet sterility standards, and must not exceed allowable endotoxin limits (ELs).
4. Parenteral solutions must meet compendial standards for particulate matter.
5. Parenteral products must be prepared in environmentally controlled areas, under strict sanitation standards, and by personnel specially trained and clothed to maintain the sanitation standards.
6. Parenteral products are packaged in special hermetic containers of specific and high quality. Special quality control procedures are used to ensure hermetic seal and sterile condition.
7. Each container of an injection is filled to a volume in slight excess of the labeled volume to be withdrawn. This overfilling permits ease of withdrawal and administration of the labeled volumes.
8. The volume of injection permitted in multiple-dose containers is restricted, as are the types of containers (single dose or multiple dose) that may be used for certain injections.
9. Specific labeling regulations apply to injections.
10. Sterile powders intended for solution or suspension immediately prior to injection are frequently packaged as lyophilized or freeze-dried powders to permit ease of solution or suspension upon the addition of the solvent or vehicle.
11. Extemporaneously prepared parenteral preparations must be compounded in a USP <797> compliant facility.

## Solvents and Vehicles for Injections

The most frequently used solvent in the large-scale manufacturer of injections is *Water for Injection, USP*. This water is purified