

Ingredients

Three general types of ingredients discussed in this section of the USP are aqueous vehicles, other vehicles, and added substances.

Aqueous vehicles must meet the requirements of the Pyrogen Test <151> or the Bacterial Endotoxins Test <85> whichever is specified. Water for injection is the vehicle unless the individual monograph specifies another aqueous vehicle.

Other vehicles refer to fixed oils that must be of vegetable origin. Oils must meet several compendial requirements, including solid paraffin (under mineral oil); a saponification value between 185 and 200 and an iodine value between 79 and 141 (fats and fixed oils <401>); and tests for unsaponifiable matter and free fatty acids. Saponification is the reaction of an ester with a metallic base and water to produce soap. It is also defined as the alkaline hydrolysis of oil or fat, or the neutralization of a fatty acid to form soap. Unsaponifiable matter is a substance that is incapable of being saponified; that is, it cannot react with a basic substance to form soap.

Added substances are formulated into injectable products to increase stability or usefulness, but must be harmless in the amounts administered and do not interfere with the therapeutic efficacy of the drug or responses to specific assays and tests. USP clearly states that no coloring agent may be added to a parenteral product. Any product with a volume of injection more than 5 mL should not use added substances unless their inclusion is clearly justified and in safe concentrations.

USP provides upper limits (unless higher limits are justified) for several specific additives:

Mercury-containing additives	0.01%
Cationic surfactants	0.01%
Chlorobutanol, cresol, phenol	0.5%
Sulfurous acid salt or equivalent	0.2%

Injections intended for multiple-dose containers must contain an additive to prevent the growth of microorganisms, regardless of the method of sterilization. Three exceptions to this rule are: (i) if there are different directions in the individual monograph; (ii) if the substance contains a radionuclide with a physical half-life of less than 24 hours; and (iii) if the active ingredient itself is antimicrobial. The antimicrobial preservative agent must meet the requirements of Antimicrobial Effectiveness Testing <51> and Antimicrobial Agents—Content <341>.

Labeling

Information that is contained on a product label includes the following:

- For liquid products: Percentage content of the drug or amount of drug in a specified volume.
- For dry products: The amount of active ingredient.
- The route of administration.
- A statement of storage conditions and an expiration date.
- The name and place of business of the manufacturer, packer, or distributor.
- Identifying lot number—The lot number is capable of yielding the complete manufacturing history of the specific package, including all manufacturing, filling, sterilizing, and labeling operations.

If the formulation is not specified in the individual monograph, the product label must contain the specific quantitative amount of each ingredient. For liquid preparations, the percentage content of each ingredient or the amount of each ingredient in a specified volume must be listed. Ingredients that are added to adjust pH or make the solution isotonic do not need to be quantified, but must be declared by name and their effect stated on the label. For dry preparations or those preparations to which a diluent will be added before use, items that must be included on the label include the following:

- The amount of each ingredient
- The composition of the recommended diluent(s)
- The amount to be used to attain a specific concentration of the active ingredient
- The final volume of the solution