

the substance under assay or test, but with the substance itself omitted.

**Change to read:**

## 2. PREPARATION AND STANDARDIZATION

### 2.1 Scope

When solutions of a reagent are used in different concentrations, the details of the preparation and standardization are usually given for the concentration most frequently required. Stronger or weaker solutions are prepared and standardized in the same general manner as described, using proportionate amounts of the reagent.

### 2.2 Preparation by dilution

It is possible in many instances to prepare lower concentrations accurately by making an exact dilution of a stronger solution.

Volumetric solutions prepared by dilution should be restandardized as directed for the stronger solution, using proportionate amounts of reagents.

Dilute solutions that are not stable, as, for instance, potassium permanganate 0.01 N, are preferably prepared by exactly diluting the higher normality with thoroughly boiled and cooled water on the same day they are required for use.

### 2.3 Standardization

The following directions give only one method for standardization, but other methods of standardization, capable of yielding at least the same degree of accuracy, may be used.

The values obtained in the standardization of volumetric solutions are valid for all Pharmacopeial uses of these solutions, regardless of the instrumental or chemical indicators used in the individual monographs.

Where the apparent normality or molarity of a titrant depends upon the special conditions of its use, the individual monograph sets forth the directions for standardizing the reagent in the specified context.

▲Primary standards are reagents that are extremely pure, stable, and have no waters of hydration. They are established by organizations such as the National Institute of Standards and Technology (NIST, [www.nist.gov](http://www.nist.gov)) in the United States, National Physical Laboratory (NPL, [www.npl.co.uk](http://www.npl.co.uk)) in the United Kingdom, etc. Some examples of primary standards are sodium carbonate, tris-(hydroxymethyl)aminomethane (TRIS or THAM), sodium chloride, potassium dichromate, and sodium tartrate. Primary standards that are used for the standardization of volumetric solutions are also known as volumetric standards. It is acceptable to use volumetric standards provided by other organizations as far as they are traceable to the appropriate primary standard. ▲USP41

For those salts that usually are available as certified primary standards or that are available as highly purified salts of primary standard quality, it is permissible to prepare solutions by accurately weighing a suitable quantity of the salt and dissolving it to produce a specific volume of solution of known concentration. ▲USP41

### 2.4 Temperature

All volumetric solutions, if practicable, are to be prepared, standardized, and used at the standard temperature of 25°.

If a titration is carried out with the volumetric solution at a markedly different temperature, standardize the volumetric

solution used as the titrant at that different temperature, or make a suitable temperature correction.

### 2 N Acetic Acid VS $C_2H_4O_2$ , 60.05 120.10 g in 1000 mL

Add 116 mL of glacial acetic acid to sufficient water to make 1000 mL after cooling to room temperature.

### 0.1 N Ammonium Thiocyanate VS $NH_4SCN$ , 76.12 7.612 g in 1000 mL

Dissolve about 8 g of ammonium thiocyanate in 1000 mL of water.

**STANDARDIZATION:** Accurately measure about 30 mL of 0.1 N silver nitrate VS into a glass-stoppered flask. Dilute with 50 mL of water, then add 2 mL of nitric acid and 2 mL of ferric ammonium sulfate TS, and titrate with the ammonium thiocyanate solution to the first appearance of a red-brown color.

$$N = \frac{\text{mL AgNO}_3 \times N \text{ AgNO}_3}{\text{mL NH}_4\text{SCN Solution}}$$

If desirable, 0.1 N ammonium thiocyanate may be replaced by 0.1 N potassium thiocyanate where the former is directed in various tests and assays.

[NOTE—If this volumetric solution is used in a qualitative application such as pH adjustment, dissolution medium, or diluent, its standardization is not required.]

### 0.05 M Barium Perchlorate VS, $Ba(ClO_4)_2$ 336.2

**DILUTED ACETIC ACID SOLUTION:** Transfer 28.5 mL of glacial acetic acid to a 100-mL volumetric flask. Dilute with water to volume.

**DILUTED AMMONIA SOLUTION:** Transfer 75 mL of stronger ammonia water to a 100-mL volumetric flask. Dilute with water to volume.

**BUFFER SOLUTION pH 3.7:** Transfer 15.0 mL of *Diluted acetic acid solution* to a 100-mL volumetric flask. Add 60 mL of alcohol and 20 mL of water. Adjust with *Diluted ammonia solution* to a pH of 3.7. Dilute with water to volume.

**DILUTED SULFURIC ACID:** Transfer 2.8 mL of sulfuric acid to a 1000-mL volumetric flask containing about 500 mL of water. Cool and dilute with water to volume.

**BARIUM PERCHLORATE SOLUTION:** Dissolve 15.8 g of barium hydroxide in a mixture of 7.5 mL of perchloric acid and 75 mL of water. Adjust with perchloric acid to a pH of 3 and filter if necessary. Add 150 mL of alcohol and dilute with water to 250 mL. Dilute with *Buffer solution pH 3.7* to 1000 mL.

**STANDARDIZATION:** To 5.0 mL of *Diluted sulfuric acid* add 5 mL of water, 50 mL of *Buffer solution pH 3.7*, and 0.5 mL of sodium alizarinsulfonate TS. Titrate with the *Barium perchlorate solution* until an orange-red color appears. Standardize immediately before use.

[NOTE—If this volumetric solution is used in a qualitative application such as pH adjustment, dissolution medium, or diluent, its standardization is not required.]

### Benzethonium Chloride, Two Hundred Fiftieth-Molar (0.004 M) $C_{27}H_{42}ClNO_2$ 448.08

Dissolve 1.792 g of benzethonium chloride, previously dried at 100°–105° to constant weight, in water to make 1000 mL.

Calculate the molarity of the solution from the content of benzethonium chloride in the dried benzethonium chloride determined as follows. Dissolve 0.350 g of the dried benzethonium chloride in 30 mL of glacial acetic acid and add 6 mL of mercuric acetate TS. Titrate with 0.1 N perchloric acid VS, using 0.05 mL of crystal violet TS as an indicator. Carry out a blank titration. One mL of 0.1 N perchloric acid VS is equivalent to 44.81 mg of benzethonium chloride ( $C_{27}H_{42}ClNO_2$ ). [NOTE—This solution is commercially available ready to be used. Use a suitable grade.]