Phosphate (Reagent test)—Cut 5 strips into small pieces, mix with 500 mg of magnesium nitrate in a porcelain crucible, and ignite. To the residue add 5 mL of nitric acid, and evaporate to dryness: the residue shows not more than 0.02 mg of PO_4.

Residue on ignition—Ignite carefully 10 strips of the paper to constant weight: the weight of the residue corresponds to not more than 0.4 mg per strip of about 3 square cm.

Rosin acids—Immerse a strip of the blue paper in a solution of 100 mg of silver nitrate in 50 mL of water: the color of the paper does not change in 30 seconds.

Sensitiveness—Drop a 10- to 12-mm strip into 100 mL of 0.0005 *N* acid contained in a beaker, and stir continuously: the color of the paper is changed within 45 seconds. The 0.0005 *N* acid is prepared by diluting 1 mL of 0.1 *N* hydrochloric acid with freshly boiled and cooled purified water to 200 mL.

Litmus Paper, Red—Usually about 6 × 50 mm in size. Red litmus paper meets the requirements of the tests for *Phosphate*, *Residue on ignition*, and *Rosin acids*, under *Litmus Paper, Blue.*

Sensitiveness—Drop a 10- to 12-mm strip into 100 mL of 0.0005 *N* sodium hydroxide contained in a beaker, and stir continuously: the color of the paper changes within 30 seconds. The 0.0005 *N* sodium hydroxide is prepared by diluting 1 mL of 0.1 *N* sodium hydroxide with freshly boiled and cooled purified water to 200 mL.

Mercuric Bromide Test Paper—Place a 50 mg/mL solution of mercuric bromide in dehydrated alcohol in a dish, and immerse in it pieces of white filter paper weighing 80 g/m^2 (speed of filtration = filtration time expressed in s for 100 mL of water at 20° with a filter surface of 10 cm^2 and a constant pressure of 6.7 kPa; 40–60 s), each measuring 1.5 cm by 20 cm and folded in the middle. Allow the excess of liquid to drain, and allow the paper to dry, protected from light, suspended over a nonmetallic thread. Discard 1 cm from each end of each strip, and cut the remainder into 1.5-cm squares or discs of 1.5-cm diameter. Store in a glass-stoppered container wrapped with black paper.

Methyl Green–Iodomercurate Paper—Immerse thin strips of suitable filter paper in a 40 g per L solution of methyl green, and allow to air-dry. Immerse the strips for 1 hour in a solution containing 140 g per L of potassium iodide and 200 g per L of mercuric iodide. Wash with water until the washings are practically colorless, and allow to air-dry. Store protected from light, and use within 48 hours.

Methyl Yellow Paper—Use a 1 in 2000 solution of methyl yellow in alcohol.

pH Indicator Paper, Short-Range—Use a suitable grade.

Phenolphthalein Paper—Use a 1 in 1000 solution of phenolphthalein in diluted alcohol.

Starch Iodate Paper—Use a mixture of equal volumes of starch TS and potassium iodate solution (1 in 20).

Starch Iodide Paper—Use a solution of 500 mg of potassium iodide in 100 mL of freshly prepared starch TS.

Thiazole Yellow Paper—Use a 1 in 2000 solution of thiazole yellow in water.

Turmeric Paper—Use a solution prepared as follows: Macerate 20 g of powdered turmeric, the dried root of *Curcuma longa* Linné (Fam. Zingiberaceae), with four 100-mL portions of cold water, decanting the clear liquid portion each time and discarding it. Dry the residue at a temperature not over 100°. Macerate with 100 mL of alcohol for several days, and filter.

Sensitiveness—Dip a strip of the paper, of about 1.5-cm length, in a solution of 1.0 mg of boric acid in 5 mL of water, previously mixed with 1 mL of hydrochloric acid. After 1 minute remove the paper from the liquid, and allow it to dry: the yellow color changes to brown. Then moisten the paper with ammonia TS: the color of the paper changes to greenish black.

Solutions

BUFFER SOLUTIONS

The successful completion of many Pharmacopeial tests and assays requires adjustment to or maintenance of a specified pH by the addition of buffer solutions. In pH measurements, standard buffer solutions are required for reference purposes. For convenience, the preparation of these solutions is in some instances described in the sections in which their use is specified; i.e., five separate phosphate buffers are described under *Antibiotics—Microbial Assays* ⟨81⟩, and several miscellaneous single-purpose solutions are described in the individual monographs.

A solution is said to be buffered if it resists changes in the activity of an ion on the addition of substances that are expected to change the activity of that ion. Buffers are substances or combinations of substances that impart this resistance to a solution. Buffered solutions are systems in which the ion is in equilibrium with substances capable of removing or releasing the ion.

Buffer capacity refers to the amount of material that may be added to a solution without causing a significant change in ion activity. It is defined as the ratio of acid or base added (in gram-equivalents per liter) to the change in pH (in pH units). The capacity of a buffered solution is adjusted to the conditions of use, usually by adjustment of the concentrations of buffer substances.

Buffers are used to establish and maintain an ion activity within narrow limits. The most common systems are used (a) to establish hydrogen-ion activity for the calibration of pH meters, (b) in the preparation of dosage forms that approach isotonicity, (c) in analytical procedures, and (d) to maintain stability of various dosage forms. Buffers used in physiological systems are carefully chosen so as not to interfere with pharmacological activity of the medicament or normal function of the organism. It is essential that buffers used in chemical analysis be compatible with the substance determined and the reagents used.

Change to read:

Standard Buffer Solutions—Standard solutions of definite pH are readily available in buffer solutions prepared from the appropriate reagents. In addition, buffer solutions, buffer tablets, and buffer solids may be obtained from commercial sources in convenient prepackaged form. Such preparations are available for the entire working range in pharmaceutical analysis, but are not recommended for pH meter standardization (see *pH* ⟨791⟩).

The required reagents are described in the section, *Reagents.* Previously dry the crystalline reagents, except the boric acid ■and sodium acetate trihydrate,■2S *(USP35)* at 110° to 120° for 1 hour.

[NOTE—Where water is specified for solution or dilution of test substances in pH determinations, use carbon dioxide-free water.]

Store the prepared solutions in chemically resistant, tight containers such as Type I glass bottles. Use the solutions within 3 months.

Standard Buffer Solutions for various ranges between pH 1.2 and 10.0 may be prepared by appropriate combinations of the solutions described herein, used in the proportions shown in the accompanying table. The volumes shown in the table are for 200 mL of buffer solution, except that the volumes shown for *Acetate Buffer* are used to prepare 1000 mL of buffer solution.

1. *Hydrochloric Acid, 0.2 M*, and *Sodium Hydroxide, 0.2 M*—Prepare and standardize as directed under *Volumetric Solutions*.
2. *Potassium Biphthalate, 0.2 M*—Dissolve 40.85 g of potassium biphthalate [$KHC_6H_4(COO)_2$] in water, and dilute with water to 1000 mL.
3. *Potassium Phosphate, Monobasic 0.2 M*—Dissolve 27.22 g of monobasic potassium phosphate (KH_2PO_4) in water, and dilute with water to 1000 mL.
4. *Boric Acid and Potassium Chloride, 0.2 M*—Dissolve 12.37 g of boric acid (H_3BO_3) and 14.91 g of potassium chloride (KCl) in water, and dilute with water to 1000 mL.
5. *Potassium Chloride, 0.2 M*—Dissolve 14.91 g of potassium chloride (KCl) in water, and dilute with water to 1000 mL.
6. *Acetic Acid, 2 N*—Prepare and standardize as directed under *Volumetric Solutions.*

Composition of Standard Buffer Solutions

Hydrochloric Acid Buffer

Place 50 mL of the potassium chloride solution in a 200-mL volumetric flask, add the specified volume of the hydrochloric acid solution, then add water to volume.

pH	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9	2.0	2.1	2.2
0.2 M HCl, mL	85.0	67.2	53.2	41.4	32.4	26.0	20.4	16.2	13.0	10.2	7.8

Acid Phthalate Buffer

Place 50 mL of the potassium biphthalate solution in a 200-mL volumetric flask, add the specified volume of the hydrochloric acid solution, then add water to volume.

pH	2.2	2.4	2.6	2.8	3.0	3.2	3.4	3.6	3.8	4.0
0.2 M HCl, mL	49.5	42.2	35.4	28.9	22.3	15.7	10.4	6.3	2.9	0.1

Neutralized Phthalate Buffer

Place 50 mL of the potassium biphthalate solution in a 200-mL volumetric flask, add the specified volume of the sodium hydroxide solution, then add water to volume.

pH	4.2	4.4	4.6	4.8	5.0	5.2	5.4	5.6	5.8
0.2 M NaOH, mL	3.0	6.6	11.1	16.5	22.6	28.8	34.1	38.8	42.3

Phosphate Buffer

Place 50 mL of the monobasic potassium phosphate solution in a 200-mL volumetric flask, add the specified volume of the sodium hydroxide solution, then add water to volume.

pH	5.8	6.0	6.2	6.4	6.6	6.8	7.0	7.2	7.4	7.6	7.8	8.0
0.2 M NaOH, mL	3.6	5.6	8.1	11.6	16.4	22.4	29.1	34.7	39.1	42.4	44.5	46.1

Alkaline Borate Buffer

Place 50 mL of the boric acid and potassium chloride solution in a 200-mL volumetric flask, add the specified volume of the sodium hydroxide solution, then add water to volume.

pH	8.0	8.2	8.4	8.6	8.8	9.0	9.2	9.4	9.6	9.8	10.0
0.2 M NaOH, mL	3.9	6.0	8.6	11.8	15.8	20.8	26.4	32.1	36.9	40.6	43.7

Acetate Buffer

Place the specified amount of sodium acetate $NaC_2H_3O_2 \cdot 3H_2O$ in a 1000-mL volumetric flask, add the specified volume of the acetic acid solution, then add water to volume, and mix.

pH	4.1	4.3	4.5	4.7	4.9	5.1	5.2	5.3	5.4	5.5
pH (measured)	4.10	4.29	4.51	4.70	4.90	5.11	5.18	5.30	5.40	5.48
$NaC_2H_3O_2 \cdot 3H_2O$, g	1.5	1.99	2.99	3.59	4.34	5.08	5.23	5.61	5.76	5.98
2 N CH_3COOH, mL	19.5	17.7	14.0	11.8	9.1	6.3	5.8	4.4	3.8	3.0

COLORIMETRIC SOLUTIONS (CS)

(For the Preparation of Matching Fluids, see *Color and Achromicity* ⟨631⟩.)

These solutions are used in the preparation of the colorimetric standards for certain drugs, and for the carbonization tests with sulfuric acid that are specified in several monographs. Store the solutions in suitably resistant, tight containers.

Comparison of colors as directed in the Pharmacopeial tests preferably is made in matched color-comparison tubes or in a suitable colorimeter under conditions that ensure that the colorimetric reference solution and that of the specimen under test are treated alike in all respects. The comparison of colors is best made in layers of equal depth, and viewed transversely against a white background (see also *Visual Comparison* under *Spectrophotometry and Light-Scattering* ⟨851⟩). It is particularly important that the solutions be compared at the same temperature, preferably 25°.

Cobaltous Chloride CS—Dissolve about 65 g of cobaltous chloride ($CoCl_2 \cdot 6H_2O$) in enough of a mixture of 25 mL of hydrochloric acid and 975 mL of water to make 1000 mL. Pipet 5 mL of this solution into a 250-mL iodine flask, add 5 mL of hydrogen peroxide TS and 15 mL of sodium hydroxide solution (1 in 5), boil for 10 minutes, cool, and add 2 g of potassium iodide and 20 mL of dilute sulfuric acid (1 in 4). When the precipitate has dissolved, titrate the liberated iodine with 0.1 N sodium thiosulfate VS, adding 3 mL of