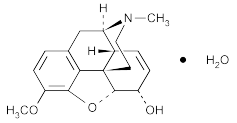
intense than that of a mixture of cobaltous chloride CS, ferric chloride CS, and water (11:76:33), in a similar bottle of the same internal diameter.

- **NONDESTEARINATED COD LIVER OIL**
  Sample: Cod Liver Oil
  Analysis: Fill a tall, cylindrical, standard oil-specimen bottle of 120-mL capacity with the *Sample* at a temperature between 23° and 28°, insert the stopper, and immerse the bottle in a mixture of ice and water for 3 h.
  Acceptance criteria: The oil remains clear and does not deposit stearin.
- **FATS AND FIXED OILS,** *Unsaponifiable Matter* ⟨**401**⟩**:** NMT 1.30%
- **FATS AND FIXED OILS,** *Acid Value* ⟨**401**⟩
  Sample solution: Mix 15 mL of alcohol with 15 mL of ether, add 5 drops of phenolphthalein TS, and neutralize with 0.1 N sodium hydroxide. Dissolve 2.0 g of Cod Liver Oil in the mixture, and boil the oil solution gently under a reflux condenser for 10 min.
  Analysis: Cool, and titrate the mixture with 0.1 N sodium hydroxide VS to the production of a pink color that persists after shaking for 30 s.
  Acceptance criteria: NMT 1.0 mL of 0.1 N sodium hydroxide is required.
- **FATS AND FIXED OILS,** *Iodine Value* ⟨**401**⟩**:** 145–180
- **FATS AND FIXED OILS,** *Saponification Value* ⟨**401**⟩**:** 180–192
  [NOTE—If carbon dioxide has been used as a preser vative, expose the Cod Liver Oil in a shallow dish in a vacuum desiccator for 24 h before weighing the specimen for determination of the saponification value.]
- **FATS AND FIXED OILS,** *Anisidine Value* ⟨**401**⟩**:** NMT 30

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers. It may be bottled or other wise packaged in containers from which air has been expelled by the production of a vacuum or by an inert gas.
- **LABELING:** The vitamin A potency and vitamin D potency, when designated on the label, are expressed in USP Units/g of oil. The potencies may be expressed also in metric units, on the basis that 1 USP V itamin A Unit equals 0.3 µg and 40 USP Vitamin D Units equals 1 µg. Where the content of docosahexaenoic acid or eicosapentaenoic acid is claimed, state the concentration in mg/g.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Cholecalciferol RS
  USP Cod Liver Oil RS
  USP Ergocalciferol RS

Codeine



$C_{18}H_{21}NO_3 \cdot H_2O$ 317.38
Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-, monohydrate, (5α,6α)-.
7,8-Didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol monohydrate [6059-47-8].
Anhydrous 299.37 [76-57-3].

» Codeine, dried at 80 ° for 4 hours, contains not less than 98.5 per cent and not more than 100.5 percent of $C_{18}H_{21}NO_3$.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Codeine Sulfate RS

Identification—

A: *Infrared Absorption* ⟨197K⟩—Proceed as directed with the codeine test specimen and the codeine standard specimen obtained from 50 mg of USP Codeine Sulfate RS dissolved in 15 mL of water, then rendered alkaline with 6 N ammonium hydroxide and extracted with several 10-mL portions of chloroform, followed by evaporation of the combined chloroform extracts on a steam bath to dr yness, and dr ying at 80° for 4 hours.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 100 µg per mL.

Medium: 0.1 N sulfuric acid.

Absorptivity at 284 nm, calculated on the dried basis, is between 112.9% and 119.9% of that of USP Codeine Sulfate RS .

Melting range ⟨741⟩**—**When previously dried, it melts between 154° and 158°, but the range between beginning and end of melting does not exceed 2 °.

Loss on drying ⟨731⟩**—**Dry it at 80 ° for 4 hours: it loses not more than 6.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Readily carbonizable substances ⟨271⟩**—**Dissolve 10 mg in 5 mL of sulfuric acid: the solution has no more color than *Matching Fluid S*.

Chromatographic purity—Prepare a solution of it in dehydrated alcohol containing 40 mg per mL (*Solution A*). Dilute 2.0 mL of *Solution A* with dehydrated alcohol to 100 mL (*Solution B*). Dilute 1.0 mL of *Solution A* with dehydrated alcohol to 100 mL (*Solution C*). Apply separate 10- µL volumes of *Solution A*, *Solution B*, and *Solution C* to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel. Allow the spots to dr y, and develop the chromatogram in a solvent system consisting of a mixture of dehydrated alcohol, cyclohexane, and ammonium hydroxide (72:30:6) until the solvent front has moved three-fourths of the length of the plate. Remove the plate from the developing chamber, and allow the solvent to evaporate. Spray the plate with a reagent prepared by mixing 3 mL of chloroplatinic acid solution (1 in 10) with 97 mL of water, followed by the addition of 100 mL of potassium iodide solution (6 in 100), and examine the chromatogram: no spot obtained from *Solution A*, other than the principal spot and any spot observed at the origin, is more intense than the principal spot obtained from *Solution B* (2%); and not more than one such spot having an R_F greater than that of the principal spot is more intense than the principal spot obtained from *Solution C* (1%).

Limit of morphine—Dissolve about 50 mg of potassium ferricyanide in 10 mL of water, and add 1 drop of ferric chloride TS and 1 mL of a neutral or slightly acid solution of Codeine (1 in 100) prepared with the aid of sulfuric acid: no blue color is produced immediately.

Assay—Dissolve about 400 mg of Codeine, previously dried and accurately weighed, by warming it in 30.0 mL of 0.1 N sulfuric acid VS. Cool, and add 10 mL of water. Add methyl red TS, and titrate the excess acid with 0.1 N sodium hydroxide VS. Perform a blank determination (see *Residual Titrations* under *Titrimetry* ⟨541⟩). Each mL of 0.1 N sulfuric acid is equivalent to 29.94 mg of $C_{18}H_{21}NO_3$.

Codeine Phosphate

$C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$ 406.37
Morphinan-6-ol, 7,8-didehydro-4,5-epoxy-3-methoxy-17-methyl-, (5α,6α)-, phosphate (1:1) (salt), hemihydrate.
7,8-Didehydro-4,5α-epoxy-3-methoxy-17-methylmorphinan-6α-ol phosphate (1:1) (salt) hemihydrate [41444-62-6].
Anhydrous 397.37 [52-28-8].

» Codeine Phosphate contains not less than 99.0 percent and not more than 101.5 per cent of $C_{18}H_{21}NO_3 \cdot H_3PO_4$, calculated on the anhydrous basis.

Packaging and storage—Preserve in tight, light-resistant containers. Store up to 40 ° as permitted by the manufacturer.

USP Reference standards ⟨11⟩**—**
USP Codeine Phosphate RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: Neutralize a solution (1 in 50) with 6 N ammonium hydroxide, and add silver nitrate TS: a yellow precipitate of silver phosphate is formed, and it is soluble in 2 N nitric acid and in 6 N ammonium hydroxide.

Acidity—Dissolve 100 mg in 20 mL of water, and titrate with 0.010 N sodium hydroxide to a pH of 5.4, using a pH meter: not more than 1.0 mL of 0.010 N sodium hydroxide is required.

Water, *Method I* ⟨921⟩**:** not more than 3.0%.

Chloride—To 10 mL of a solution (1 in 100), acidified with nitric acid, add a few drops of silver nitrate TS: no opalescence is produced immediately.

Sulfate—To 10 mL of a solution (1 in 100) add a few drops of barium chloride TS: no turbidity is produced immediately.

Limit of morphine—Dissolve about 50 mg of potassium ferricyanide in 10 mL of water, and add 1 drop of ferric chloride TS and 1 mL of a solution of Codeine Phosphate (1 in 100): no blue color is produced immediately.

Chromatographic purity—Using Codeine Phosphate, proceed as directed in the test for *Chromatographic purity* under *Codeine,* except to use a mixture of 0.01 N hydrochloric acid and dehydrated alcohol (4:1), instead of dehydrated alcohol, to prepare *Solution A, Solution B,* and *Solution C.*

Assay—Dissolve about 1 g of Codeine Phosphate, accurately weighed, in 50 mL of glacial acetic acid, warming slightly if necessary to effect solution, and titrate with 0.1 N perchloric acid VS, determining the endpoint potentiometrically. Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 39.74 mg of $C_{18}H_{21}NO_3 \cdot H_3PO_4$.

Codeine Phosphate Injection

» Codeine Phosphate Injection is a sterile solution of Codeine Phosphate in Water for Injection. It contains not less than 93.0 per cent and not more than 107.0 per cent of the labeled amount of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$.
NOTE—Do not use the Injection if it is more than slightly discolored or contains a precipitate.

Packaging and storage—Preserve in single-dose or multiple-dose containers, preferably of Type I glass, protected from light.

USP Reference standards ⟨11⟩**—**
USP Codeine Phosphate RS
USP Endotoxin RS

Identification—

A: Dilute a volume of Injection, equivalent to about 90 mg of codeine phosphate, with water to about 10 mL, add 1 drop of hydrochloric acid, and extract with three 10-mL portions of chloroform, discarding the chloroform extracts. Add 6 N ammonium hydroxide until the solution is alkaline, and extract with several 10-mL portions of chloroform. Evaporate the combined chloroform extracts on a steam bath to dryness, and dry at 80 ° for 4 hours: the IR absorption spectrum of a potassium bromide dispersion of the residue so obtained exhibits maxima at the same wavelengths as that of the codeine obtained by similarly treating 1 mL of a solution of USP Codeine Phosphate RS (1 in 100).

B: A volume of Injection, equivalent to about 60 mg of codeine phosphate, responds to *Identification* test *B* under *Codeine Phosphate*.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 5.8 USP Endotoxin Units per mg of codeine phosphate.

pH ⟨791⟩: between 3.0 and 6.0.

Limit of morphine—Diluted with water to a concentration of 5 mg of codeine phosphate per mL, it meets the requirements of the test for *Limit of morphine* under *Codeine Phosphate*.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—Transfer an accurately measured volume of Injection, equivalent to about 75 mg of codeine phosphate, to a small separator, and add about 15 mL of water. Add 2 drops of phosphoric acid, and extract with four 10-mL portions of chloroform, collecting the chloroform extracts in a separator. Wash the combined chloroform extracts with 10 mL of water, and add the water wash to the first separator containing the sample. Discard the chloroform extracts. Proceed as directed in the *Assay* under *Codeine Phosphate Tablets*, beginning with "render the solution alkaline with 6 N ammonium hydroxide." Each mL of 0.02 N sulfuric acid is equivalent to 8.128 mg of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$.

Codeine Phosphate Tablets

» Codeine Phosphate Tablets contain not less than 93.0 percent and not more than 107.0 percent of the labeled amount of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$.

Packaging and storage—Preserve in well-closed, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Codeine Phosphate RS

Identification—

A: Digest a quantity of finely powdered Tablets, equivalent to about 100 mg of codeine phosphate, with 15 mL of water and 5 mL of 2 N sulfuric acid for 1 hour. Filter, if necessary, and wash any undissolved residue with a few mL of water. Render the filtrate alkaline with 6 N ammonium hydroxide, extract with several small portions of chloroform, and proceed as directed in *Identification* test *A* under *Codeine Phosphate Injection*, beginning with "Evaporate the combined chloroform extracts." The specified results are observed.

B: To a quantity of finely powdered Tablets, equivalent to about 100 mg of codeine phosphate, add 10 mL of water and 2 drops of 2 N sulfuric acid. Digest, with frequent shaking, for 15 minutes, and filter. Neutralize 5 mL of the filtrate with 6 N ammonium hydroxide, and add silver nitrate TS: a yellow precipitate of silver phosphate is formed, and it is soluble in diluted nitric acid and in 6 N ammonium hydroxide.

Dissolution ⟨711⟩**—**

Medium: water; 900 mL.

Apparatus 2: 50 rpm.

Time: 45 minutes.

Procedure—Determine the amount of $C_{18}H_{21}NO_3 \cdot H_3PO_4 \cdot {}^1/_2H_2O$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 284 nm on filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution hav-