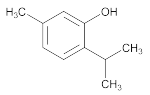
Sample solution: 200 mg/mL in water
- **LOSS ON DRYING ⟨731⟩:** Dry over phosphorus pentoxide for 3 h: it loses NMT 0.5% of its weight.
- **LIMIT OF OXALATE**
  Sample solution: 10 mL of a 1-in-10 solution of Tartaric Acid
  Analysis: Nearly neutralize the *Sample solution* with 6 N ammonium hydroxide, and add 10 mL of calcium sulfate TS.
  Acceptance criteria: No turbidity is produced.

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Tartaric Acid RS

Thimerosal—*see Thimerosal General Monographs*

Thymol



$C_{10}H_{14}O$ 150.22
Phenol, 5-methyl-2-(1-methylethyl)-;
Thymol;
p-Cymen-3-ol [89-83-8].

DEFINITION
Thymol contains NLT 99.0% and NMT 101.0% of thymol ($C_{10}H_{14}O$).

IDENTIFICATION
- **A. INFRARED ABSORPTION ⟨197K⟩**
- **B.** It meets the requirements in *Specific Tests* for *Melting Range or Temperature* ⟨741⟩.

ASSAY
- **PROCEDURE**
  Sample: 100 mg
  Titrimetric system
  (See *Titrimetry* ⟨541⟩.)
  Mode: Direct titration
  Titrant: 0.1 N bromine VS
  Endpoint detection: Visual
  Analysis: Transfer the *Sample* to a 250-mL iodine flask, and dissolve in 25 mL of 1 N sodium hydroxide. Add 20 mL of hot dilute hydrochloric acid (1 in 2), and immediately titrate with *Titrant* to within 1–2 mL of the calculated endpoint. Warm the solution to between 70° and 80°, add 2 drops of methyl orange TS, and continue the titration slowly, swirling vigorously after each addition. When the color of the methyl orange is bleached, add 2 drops of *Titrant*, shake for 10 s, add 1 drop of methyl orange TS, and shake vigorously. If the solution is red, continue the titration, dropwise and with shaking, until the color is discharged. Repeat the alternate addition of the *Titrant* and methyl orange TS until the red color is discharged after the addition of the methyl orange TS. Each mL of *Titrant* is equivalent to 3.755 mg of thymol ($C_{10}H_{14}O$).
  Acceptance criteria: 99.0%–101.0%

IMPURITIES
- **LIMIT OF NONVOLATILE RESIDUE**
  Sample: 2 g
  Analysis: Volatilize the *Sample* on a steam bath, and dry at 105° to constant weight.
  Acceptance criteria: NMT 0.05%

SPECIFIC TESTS
- **MELTING RANGE OR TEMPERATURE ⟨741⟩:** 48°–51°; but when melted, Thymol remains liquid at a considerably lower temperature.

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.
- **USP REFERENCE STANDARDS ⟨11⟩**
  USP Thymol RS

Titanium Dioxide—*see Titanium Dioxide General Monographs*

Tocopherols Excipient

DEFINITION
Tocopherols Excipient is a vegetable oil solution containing NLT 50.0% of total tocopherols, of which NLT 80.0% consists of varying amounts of beta, gamma, and delta tocopherols.

IDENTIFICATION
- **A.**
  Sample solution: 50 mg of Tocopherols Excipient in 10 mL of dehydrated alcohol
  Analysis: To the *Sample solution* add with swirling 2 mL of nitric acid, and heat at about 75° for 15 min.
  Acceptance criteria: A bright red or orange color develops.
- **B.** The retention time of the third major peak (i.e., the peak occurring just before that of the internal standard) of the *Sample solution* corresponds to that of the *Standard solution*, both relative to that of the internal standard, as obtained in the *Assay*.

ASSAY
- **PROCEDURE**
  Solution A: Pyridine and propionic anhydride (2:1)
  Internal standard solution: 3 mg/mL of hexadecyl hexadecanoate in *Solution A*
  Standard solutions: Using low-actinic glassware, add 12-, 25-, 37-, and 50-mg portions of USP Alpha Tocopherol RS to separate 50-mL conical flasks having 19/38 standard-taper ground-glass necks. Pipet 25 mL of the *Internal standard solution* into each flask, and reflux for 10 min under water-cooled condensers.
  Sample solution: Using low-actinic glassware, add 60 mg of Tocopherols Excipient to a 50-mL conical flask similar to the flasks used in preparing the *Standard solutions*. Add 10.0 mL of *Internal standard solution*, and reflux for 10 min under a water-cooled condenser.
  Chromatographic system
  (See *Chromatography* ⟨621⟩*, System Suitability*.)
  Mode: GC
  Detector: Flame ionization
  Column: 4-mm × 2-m borosilicate glass; packed with 2%–5% liquid phase G2 on 80- to 100-mesh support S1AB using either a glass-lined sample introduction system or on-column injection

Temperatures
Column: 245°–265°, maintained isothermally
Injection port: 10° higher than the *Column* temperature
Detector: 10° higher than the *Column* temperature
Flow rate: Dry carrier gas is adjusted to obtain a hexadecyl hexadecanoate peak 30–32 min after sample introduction. [NOTE—Cure and condition the column as necessary.]
Injection volume: 2–5 µL
System suitability
Sample: *Sample solution*
[NOTE—The relative retention times for delta tocopheryl propionate, beta plus gamma tocopheryl propionate, and hexadecyl hexadecanoate are about 0.50, 0.63, and 1.00, respectively.]
Suitability requirements
Resolution: Chromatograph a sufficient number of injections to ensure that a resolution of NLT 2.5 between delta tocopheryl propionate and beta plus gamma tocopheryl propionate relative to hexadecyl hexadecanoate is met.
Analysis
Samples: *Standard solutions* and *Sample solution*
Calibration: Chromatograph each *Standard solution*, and calculate the relative response factor, *F*, for each concentration of the *Standard solution* taken:

$$F = (r_S/r_D) \times (C_D/C_S)$$

r_S = peak response of alpha tocopherol in the *Standard solution*
r_D = peak response of hexadecyl hexadecanoate in the *Standard solution*
C_D = concentration of hexadecyl hexadecanoate in the *Standard solution* (mg/mL)
C_S = concentration of USP Alpha Tocopherol RS in the *Standard solution* (mg/mL)

Chromatograph a sufficient number of injections of each *Standard solution* to ensure that *F* is constant within a range of 2.0%. Prepare a relative response factor curve by plotting *F* versus the alpha tocopheryl propionate peak response.
Inject the *Sample solution*, and measure the responses for the four major peaks occurring at relative retention times of approximately 0.50, 0.63, 0.76, and 1.00, and record the values as a_δ, $a_{\beta\gamma}$, a_α, and a_D, corresponding to delta tocopheryl propionate, beta plus gamma tocopheryl propionates, alpha tocopheryl propionate, and hexadecyl hexadecanoate, respectively.
Calculate the quantity of each tocopherol form in the Tocopherols Excipient taken:

$$\text{delta tocopherol} = (V \times C_D/F) \times (a_\delta/a_D)$$

$$\text{beta plus gamma tocopherols} = (V \times C_D/F) \times (a_{\beta\gamma}/a_D)$$

$$\text{alpha tocopherol} = (V \times C_D/F) \times (a_\alpha/a_D)$$

V = volume of *Internal standard solution* used in the *Sample solution* (mL)
F = obtained from the relative response factor curve (see *Calibration*) for each of the corresponding responses for the delta, beta plus gamma, and alpha tocopheryl propionate peaks produced by the *Sample solution*

[NOTE—The relative response factor for delta tocopheryl propionate and for beta plus gamma tocopheryl propionates has been determined empirically to be the same as for alpha tocopheryl propionate.]

Acceptance criteria: NLT 50.0% of total tocopherols, of which NLT 80.0% consists of varying amounts of beta, gamma, and delta tocopherols

SPECIFIC TESTS
- **ACIDITY**
Solution A: Alcohol and ether (50%:50%). Neutralize to phenolphthalein with 0.1 N sodium hydroxide.
Sample solution: Dissolve 1.0 g of Tocopherols Excipient in 25 mL of *Solution A*.
Analysis: To the *Sample solution* add 0.5 mL of phenolphthalein TS, and titrate with 0.10 N sodium hydroxide until the solution remains faintly pink after being shaken for 30 s.
Acceptance criteria: NMT 1.0 mL of 0.10 N sodium hydroxide is required.

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight containers, protected from light. Protect with a blanket of an inert gas.
- **LABELING:** Label it to indicate the content, in mg/g, of total tocopherols and of the sum of beta, gamma, and delta tocopherols.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Alpha Tocopherol RS

Tolu Balsam Syrup

DEFINITION
Prepare Tolu Balsam Syrup as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Tolu Balsam Tincture	50 mL
Magnesium Carbonate	10 g
Sucrose	820 g
Purified Water, a sufficient quantity to make	1000 mL

Add the *Tincture* all at once to the *Magnesium Carbonate* and 60 g of the *Sucrose* in a mortar, and mix. Gradually add 430 mL of *Purified Water* with trituration, and filter. Dissolve the remainder of the *Sucrose* in the clear filtrate with gentle heating, strain the syrup while warm, and add sufficient *Purified Water* through the strainer to make the product measure 1000 mL, and mix.
Tolu Balsam Syrup may also be prepared as follows. Place 760 g of the *Sucrose* in a suitable percolator, the neck of which is nearly filled with loosely packed cotton, moistened after packing with a few drops of water. Pour the filtrate, obtained as directed in the preceding instructions, on the *Sucrose*, and regulate the outflow to a steady drip of percolate. When all of the liquid has run through, return portions of the percolate, if necessary, to dissolve all the *Sucrose*. Then pass enough *Purified Water* through the cotton to make the product measure 1000 mL, and mix.

OTHER COMPONENTS
- **ALCOHOL DETERMINATION,** *Method II* ⟨**611**⟩**:** 3.0%–5.0%

SPECIFIC TESTS
- **FATS AND FIXED OILS,** *Acid Value* ⟨**401**⟩
Sample solution: 2% of solution
Analysis: Add phenolphthalein TS, and titrate with 0.5 N alcoholic potassium hydroxide VS.
Acceptance criteria: 112–168

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Package in tight containers, and store at controlled room temperature.