Mode: LC
Detector: UV 280 nm
Column: 4.6-mm × 15-cm; packing L1
Flow rate: 1 mL/min
Injection size: 25 µL
System suitability
Sample: *Standard solution*
[NOTE—The relative retention times for ethylparaben and ethinyl estradiol are about 0.6 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 4.5 between the ethylparaben and ethinyl estradiol peaks
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of ethinyl estradiol ($C_{20}H_{24}O_2$) taken:

$$\text{Result} = (R_U/R_S) \times (C_S/C_U) \times 100$$

R_U = peak response ratio from the *Sample solution*
R_S = peak response ratio from the *Standard solution*
C_S = concentration of USP Ethinyl Estradiol RS in the *Standard solution* (mg/mL)
C_U = concentration of Ethinyl Estradiol in the *Sample solution* (mg/mL)
Acceptance criteria: 97.0%–102.0% on the dried basis

IMPURITIES
• **COMPLETENESS OF SOLUTION:** Dissolve 100 mg in 5 mL of alcohol; the solution is clear and free from undissolved solid.

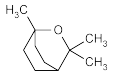
SPECIFIC TESTS
• **MELTING RANGE OR TEMPERATURE ⟨741⟩:** 180°–186°. It may exist also in a polymorphic modification, melting at 142°–146°.

Change to read:

• **OPTICAL ROTATION,** *Specific Rotation* **⟨781S⟩**
Sample solution: ■50 mg/mL, using sonication if necessary, in colorless pyridine from a freshly opened container■1S *(USP35)*
Acceptance criteria: –28.0° to –29.5°
• **LOSS ON DRYING ⟨731⟩:** Dry a sample at 105° for 3 h: it loses NMT 1.0% of its weight.

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

Eucalyptol



$C_{10}H_{18}O$ 154.25
1,3,3-Trimethyl-2-oxabicyclo[2.2.2]octane;
1,8-Epoxy-*p*-menthane [470-82-6].

DEFINITION
Eucalyptol is obtained from oil of eucalyptus and from other sources. It contains NLT 98.0% and NMT 100.0% of $C_{10}H_{18}O$.

IDENTIFICATION

Add the following:

■• **A. INFRARED ABSORPTION ⟨197F⟩**■1S *(USP35)*

Change to read:

• ■**B.**■1S *(USP35)* Add 1 mL of phosphoric acid to 1 mL of Eucalyptol contained in a test tube maintained in an ice bath. A solid white crystalline mass is formed, from which eucalyptol separates upon addition of warm water.

ASSAY
• **PROCEDURE**
System suitability solution: 0.2 mg/mL of limonene and 0.9 mg/mL of USP Eucalyptol RS in methanol
Sample solution: 0.9 mg/mL of Eucalyptol in methanol
Blank: Methanol
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: GC
Detector: Flame ionization
Column: 0.32-mm × 60-m fused-silica capillary column coated with phase G16
Temperature
Injector port: 250°
Detector: 250°
Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
60	6	200	—

Split flow rate: 50 mL/min
Carrier gas: Helium
Column head pressure: 30 psi
Injection size: 1 µL
System suitability
Sample: *System suitability solution*
Suitability requirements
Resolution: NLT 2.0 between limonene and eucalyptol
Column efficiency: NLT 150,000 theoretical plates, eucalyptol
Analysis
Samples: *Sample solution* and *Blank*
[NOTE—Identify any peaks from the *Sample solution* that correspond to those in the *Blank* by their retention times.]
Calculate the percentage of eucalyptol ($C_{10}H_{18}O$) in the portion of Eucalyptol taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of eucalyptol from the *Sample solution*
r_T = sum of all peak responses from the *Sample solution*, other than the responses corresponding to those of the *Blank*
Acceptance criteria: 98.0%–100.0%

IMPURITIES
• **LIMIT OF PHENOLS**
Analysis 1: Shake 5 mL with 5 mL of sodium hydroxide TS.
Acceptance criteria 1: The volume of Eucalyptol is not diminished.

Analysis 2: Shake 1 mL with 20 mL of water and allow the liquids to separate. To 10 mL of the water layer add 1 drop of ferric chloride TS.
Acceptance criteria 2: The mixture develops no violet color.

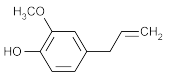
SPECIFIC TESTS
- **SPECIFIC GRAVITY ⟨841⟩:** 0.921–0.924
- **CONGEALING TEMPERATURE ⟨651⟩:** NLT 0°
- **OPTICAL ROTATION,** *Angular Rotation* **⟨781A⟩:** –0.5° to +0.5°
- **DISTILLING RANGE,** *Method I* **⟨721⟩:** 174°–177°
- **REFRACTIVE INDEX ⟨831⟩:** 1.455–1.460 at 20°

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight containers.

Add the following:

■• **USP REFERENCE STANDARDS ⟨11⟩**
USP Eucalyptol RS■1S *(USP35)*

Eugenol



$C_{10}H_{12}O_2$ 164.20
Phenol, 2-methoxy-4-(2-propenyl)-;
4-Allyl-2-methoxyphenol [97-53-0].

DEFINITION
Eugenol is obtained from clove oil and from other sources.

IDENTIFICATION

Add the following:

■• **A. INFRARED ABSORPTION ⟨197F⟩**■1S *(USP35)*

IMPURITIES
- **HEAVY METALS,** *Method II* **⟨231⟩:** NMT 40 ppm
- **HYDROCARBONS**
Analysis: Dissolve 1 mL in 20 mL of 0.5 N sodium hydroxide in a 50-mL stoppered tube, add 18 mL of water, and mix.
Acceptance criteria: A clear mixture results immediately, but it may become turbid when exposed to air.
- **LIMIT OF PHENOL**
Analysis: Shake 1 mL with 20 mL of water. Filter, and add 1 drop of ferric chloride TS to 5 mL of the clear filtrate.
Acceptance criteria: The mixture exhibits a transient grayish-green color but not a blue or violet color.

SPECIFIC TESTS
- **SPECIFIC GRAVITY ⟨841⟩:** 1.064–1.070
- **DISTILLING RANGE,** *Method II* **⟨721⟩:** NLT 95% distills from 250°–255°
- **REFRACTIVE INDEX ⟨831⟩:** 1.540–1.542 at 20°
- **SOLUBILITY IN 70% ALCOHOL:** One volume dissolves in 2 volumes of 70% alcohol.

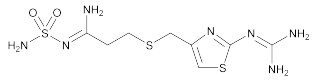
ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers.

Add the following:

■• **USP REFERENCE STANDARDS ⟨11⟩**
USP Eugenol RS■1S *(USP35)*

Famotidine

Change to read:



$C_8H_{15}N_7O_2S_3$ 337.45
Propanimidamide, *N'*-(aminosulfonyl)-3-[[[2-[(diaminomethylene)amino]-4-thiazolyl]methyl]thio]-;
[1-Amino-3-[[[2-[(diaminomethylene)amino]-4-thiazolyl]methyl]thio]propylidene]sulfamide;
■3-[[2-(Diaminomethyleneamino)thiazol-4-yl]methylthio]-*N'*-sulfamoylpropanimidamide■1S *(USP35)* [76824-35-6].

DEFINITION
Famotidine contains NLT 98.5% and NMT 101.0% of famotidine ($C_8H_{15}N_7O_2S_3$), calculated on the dried basis.

IDENTIFICATION
- **A. INFRARED ABSORPTION ⟨197K⟩**

Delete the following:

■• **B. ULTRAVIOLET ABSORPTION ⟨197U⟩**
Analytical wavelength: 265 nm
Buffer: Adjust 250 mL of 0.02 M phosphoric acid with a 100 mg/mL sodium hydroxide solution to a pH of 2.5, and dilute with water to 500 mL.
Sample solution: 25 µg/mL in *Buffer*
Acceptance criteria: The absorptivities, calculated on the dried basis, do not differ by more than 3.0%.■1S *(USP35)*

ASSAY

Change to read:

- **PROCEDURE**
Sample: Dissolve 250 mg of Famotidine in 80 mL of glacial acetic acid.
Analysis: Titrate with 0.1 N perchloric acid VS (see *Titrimetry* ⟨541⟩), using a suitable anhydrous electrode system.■■1S *(USP35)* Perform a blank determination, and make any necessary correction. Each mL of 0.1 N perchloric acid is equivalent to 16.87 mg of $C_8H_{15}N_7O_2S_3$.
Acceptance criteria: 98.5%–101.0% on the dried basis

IMPURITIES
- **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%
- **HEAVY METALS,** *Method II* **⟨231⟩:** NMT 10 ppm

Delete the following:

■• **CHROMATOGRAPHIC PURITY**
Adsorbent: 0.25-mm layer of chromatographic silica gel mixture
Sample solution: Transfer 200 mg of Famotidine to a 10-mL volumetric flask. Add 2 mL of methanol, and shake for 10 min. Add 0.1 mL of glacial acetic acid, stir until dissolved, and dilute with methanol to volume.
Standard solution A: 0.2 mg/mL of USP Famotidine RS in methanol and glacial acetic acid (100:1)