Identified Ethyl Ester	Relative Retention Time
C18:3 n-3	0.585
C18:4 n-3	0.608
C18:4 n-1	0.618
Furan acid 5	0.691
C19:5	0.710
C20:3 n-6	0.720
C20:4 n-6	0.736
Furan acid 7	0.744
C20:4 n-3	0.777
Furan acid 8	0.783
EPA	0.796
Furan acid 9	0.867
C21:5 n-3	0.889
C22:4	0.917
Furan acid 10	0.922
C22:5 n-6	0.939
Furan acid 11	0.963
C22:5 n-3	0.977
DHA	1.000

Calculate the content of unidentified fatty acids ethyl esters in area percentage:

$$\text{Result} = 100 - (100 \times \Sigma\, \text{Aiee}/r_T)$$

Aiee = peak area for each identified ethyl ester in the table above

r_T = sum of the areas of all peaks except solvents, BHT, and internal standard

Acceptance criteria: The area of the largest single unidentified peak is NMT 0.5% of the total area. The total area of unidentified peaks as calculated above is NMT 2%.

SPECIFIC TESTS

- **FATS AND FIXED OILS** ⟨**401**⟩**,** *Acid Value***:** NMT 2.0 mg of KOH/g
- **FATS AND FIXED OILS** ⟨**401**⟩**,** *Anisidine Value***:** NMT 15
- **FATS AND FIXED OILS** ⟨**401**⟩**,** *Peroxide Value***:** NMT 10.0
- **ABSORBANCE**

  Sample solution: Transfer 300 mg, accurately weighed, into a 50-mL volumetric flask. Dissolve in, and dilute immediately with isooctane to volume. Pipet 2.0 mL into a 50-mL volumetric flask, and dilute with isooctane to volume.

  Acceptance criteria: NMT 0.55, determined at 233 nm, with isooctane being used as the blank

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers under a nitrogen atmosphere. Store at controlled room temperature.
- **LABELING:** The label states the content of DHA ethyl ester and EPA ethyl ester in mg/g, the sum of the EPA and DHA ethyl esters contents in mg/g, and the content of the total omega-3-acid ethyl esters in percentage (w/w). It also states the name of any added antioxidant.
- **USP REFERENCE STANDARDS** ⟨**11**⟩

  USP Alpha Tocopherol RS

  USP Docosahexaenoic Acid Ethyl Ester RS

  All *cis*-4,7,10,13,16,19-docosahexaenoic ethyl ester.

  $C_{24}H_{36}O_2$ 356.55

  USP Eicosapentaenoic Acid Ethyl Ester RS

  all *cis*-5,8,11,14,17-Eicosapentaenoic ethyl ester.

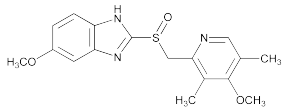
  $C_{22}H_{34}O_2$ 330.51

  USP Methyl Tricosanoate RS

  Tricosanoic acid methyl ester.

  $C_{24}H_{48}O_2$ 368.64

Omeprazole



$C_{17}H_{19}N_3O_3S$ 345.42

1*H*-Benzimidazole, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-.

5-Methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]benzimidazole [73590-58-6].

» Omeprazole contains not less than 98.0 percent and not more than 102.0 percent of $C_{17}H_{19}N_3O_3S$, calculated on the dried basis.

Packaging and storage—Preserve in tight containers and store in a cold place, protected from moisture.

USP Reference standards ⟨11⟩**—**
USP Omeprazole RS

Identification—

A: The R_F value of the principal spot observed in the chromatogram of the *Identification solution* corresponds to that of the principal spot observed in the chromatogram of the *Standard solution* containing 0.15 mg of USP Omeprazole RS per mL, obtained as directed in the test for *Chromatographic purity, Method 1.*

B: *Infrared Absorption* ⟨197K⟩.

Completeness of solution ⟨641⟩**:** meets the requirements, a solution in methylene chloride containing 20 mg per mL being used.

Color of solution—Determine the absorbance of the solution prepared for the *Completeness of solution* test at 440 nm, in 1-cm cells, using methylene chloride as the blank: the absorbance is not greater than 0.10.

Loss on drying ⟨731⟩**—**Dry it in vacuum at 60° for 4 hours: it loses not more than 0.5% of its weight.

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

Heavy metals, *Method II* ⟨231⟩**:** 0.002%.

Chromatographic purity—

METHOD 1—

Solvent—Prepare a mixture of dichloromethane and methanol (1:1).

Standard solutions—Dissolve an accurately weighed quantity of USP Omeprazole RS in *Solvent,* and mix to obtain *Standard solution A* having a known concentration of about 0.5 mg per mL. Dilute this solution quantitatively with *Solvent* to obtain *Standard solution B* and *Standard solution C* having known concentrations of about 0.15 mg per mL and 0.05 mg per mL, respectively.

Test solution—Prepare a solution of Omeprazole in *Solvent* containing 50 mg per mL.

Identification solution—Dilute a volume of the *Test solution* quantitatively with *Solvent* to obtain a solution containing 0.25 mg per mL.

Procedure—Separately apply 10 µL of the *Test solution,* the *Identification solution,* and each of the *Standard solutions* to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of ammonia-saturated dichloromethane, dichloromethane, and isopropyl alcohol (2:2:1) until the solvent front has moved about three-fourths of the length of the plate. [NOTE—Prepare ammonia-saturated dichloromethane as follows. Shake 100 mL of dichloromethane with 30 mL of ammonium hydroxide in a separatory funnel, allow the layers to separate, and use the lower layer.] Remove the plate from the developing chamber, mark the solvent front,

allow the solvent to evaporate, and examine the plate under short-wavelength UV light: the chromatograms show principal spots at about the same R_F value. Estimate the intensities of any secondary spots observed in the chromatogram of the *Test solution* by comparison with the spots in the chromatograms of the *Standard solutions:* no secondary spot from the chromatogram of the *Test solution* is larger or more intense than the principal spot obtained from *Standard solution B* (0.3%), and the sum of the intensities of all secondary spots obtained from the *Test solution* is not more intense than the principal spot obtained from *Standard solution A* (1.0%).

METHOD 2—

Diluent—Use *Mobile phase.*

Phosphate buffer, Mobile phase, System suitability solution, and *Chromatographic system*—Proceed as directed in the *Assay.*

Test solution—Dissolve an accurately weighed quantity of Omeprazole in *Diluent* to obtain a solution containing about 0.16 mg per mL. [NOTE—Prepare this solution fresh.]

Procedure—Inject equal volumes (about 40 µL) of the *Test solution* and *Diluent* into the chromatograph, and allow the *Test solution* to elute for not less than two times the retention time of omeprazole. Record the chromatograms, and measure the peak responses. Calculate the percentage of each impurity in the portion of Omeprazole taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak response for each impurity, and r_s is the sum of the responses of all of the peaks: not more than 0.3% of any individual impurity is found, and the sum of all impurities is not more than 1.0%.

Assay—

Phosphate buffer—Dissolve 0.725 g of monobasic sodium phosphate and 4.472 g of anhydrous dibasic sodium phosphate in 300 mL of water, dilute with water to 1000 mL, and mix. Dilute 250 mL of this solution with water to 1000 mL. If necessary, adjust the pH with phosphoric acid to 7.6.

Mobile phase—Prepare a filtered and degassed mixture of *Phosphate buffer* and acetonitrile (3:1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a mixture of 0.01 M sodium borate and acetonitrile (3:1).

Standard preparation—Dissolve an accurately weighed quantity of USP Omeprazole RS in *Diluent,* and dilute quantitatively, and stepwise if necessary, with *Diluent* to obtain a solution having a known concentration of about 0.2 mg per mL.

Assay preparation—Transfer about 100 mg of Omeprazole, accurately weighed, to a 50-mL volumetric flask, dissolve in and dilute with *Diluent* to volume, and mix. Transfer 5.0 mL of this solution to a 50-mL volumetric flask, dilute with *Diluent* to volume, and mix.

System suitability solution—Dilute a volume of *Standard preparation* with *Diluent* to obtain a solution containing about 0.1 mg of USP Omeprazole RS per mL.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 280-nm detector and a 4.6-mm × 15-cm column that contains 5-µm packing L7. The flow rate is about 0.8 mL per minute. Chromatograph the *System suitability solution,* and record the peak responses as directed for *Procedure:* the capacity factor, k', is not less than 6.0; the column efficiency is not less than 3000 theoretical plates; the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{17}H_{19}N_3O_3S$ in the portion of Omeprazole taken by the formula:

$$500C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of USP Omeprazole RS in the *Standard preparation;* and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Omeprazole Delayed-Release Capsules

» Omeprazole Delayed-Release Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of omeprazole ($C_{17}H_{19}N_3O_3S$).

Packaging and storage—Preserve in tight, light-resistant containers. Store between 15° and 30°.

Labeling—When more than one *Dissolution Test* is given, the labeling states the *Dissolution Test* used only if *Test 1* is not used.

USP Reference standards ⟨11⟩**—**
USP Omeprazole RS

Identification— The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Dissolution ⟨711⟩**—**

TEST 1—

ACID RESISTANCE STAGE—

Medium: 0.1 N hydrochloric acid; 500 mL.

Apparatus 2: 100 rpm.

Time: 2 hours.

pH 7.6 Phosphate buffer, Mobile phase, and *Chromatographic system*—Proceed as directed for *Buffer stage.*

Standard solution—Transfer about 50 mg of USP Omeprazole RS, accurately weighed, to a 250-mL volumetric flask, dissolve in 50 mL of alcohol, dilute with 0.01 M sodium borate solution to volume, and mix. Transfer 10.0 mL of this solution into a 100-mL volumetric flask, add 20 mL of alcohol, dilute with 0.01 M sodium borate solution to volume, and mix.

Test solution—After 2 hours, filter the *Medium* containing the pellets through a sieve with an aperture of not more than 0.2 mm. Collect the pellets on the sieve, and rinse them with water. Using approximately 60 mL of 0.01 M sodium borate solution, carefully transfer the pellets quantitatively to a 100-mL volumetric flask. Sonicate for about 20 minutes until the pellets are broken up. Add 20 mL of alcohol to the flask, dilute with 0.01 M sodium borate solution to volume, and mix. Dilute an appropriate amount of this solution with 0.01 M sodium borate solution to obtain a solution having a concentration of about 0.02 mg per mL. At level L_1, test 6 units. Test 6 additional units at level L_2, and at level L_3, an additional 12 units are tested. Continue testing through the three levels unless the results conform at either L_1or L_2.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of omeprazole ($C_{17}H_{19}N_3O_3S$) dissolved in the *Medium* by the formula:

$$T - CD(r_U / r_S)$$

in which T is the labeled quantity, in mg, of omeprazole in the capsule; C is the concentration, in mg per mL, of USP Omeprazole RS in the *Standard solution; D* is the dilution factor used in preparing the *Test solution;* and r_U and r_S are the omeprazole