Packaging and storage—Preserve in tight containers.

Identification—

A: To 5 mL of a solution (1 in 20) add 5 mL of sodium hydroxide TS. Boil for a few minutes, cool, and acidify with 3 N hydrochloric acid: the solution is strongly opalescent.

B: To 2 mL of a solution (1 in 20) add 0.5 mL of bromine TS, dropwise: the bromine is not decolorized (*distinction from Polysorbate 80*).

C: A mixture of 60 volumes of it and 40 volumes of water yields a gelatinous mass at normal and lower than normal room temperatures.

Hydroxyl value ⟨401⟩: between 89 and 105.

Saponification value ⟨401⟩: between 41 and 52.

Acid value—Weigh 10.0 g into a wide-mouth, 250-mL conical flask, and add 50 mL of neutralized alcohol. Heat on a steam bath nearly to boiling, shaking thoroughly occasionally while heating. Invert a beaker over the mouth of the flask, cool under running water, add 5 drops of phenolphthalein TS, and titrate with 0.1 N sodium hydroxide VS: not more than 4 mL of 0.100 N sodium hydroxide is required, corresponding to an acid value of 2.2.

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

Residue on ignition ⟨281⟩**:** not more than 0.25%.

Heavy metals, *Method II* ⟨231⟩**:** 0.001%.

Polysorbate 60

Sorbitan, monooctadecanoate, poly(oxy-1,2-ethanediyl) derivs.; Polyoxyethylene 20 sorbitan monostearate
[Compound usually also contains associated fatty acids.] [9005-67-8].

DEFINITION

Polysorbate 60 is a mixture of stearate and palmitate esters of sorbitol and its anhydrides copolymerized with about 20 moles of ethylene oxide for each mole of sorbitol and sorbitol anhydrides.

IDENTIFICATION

- **A.**
  Sample solution: 1 in 20, in water
  Analysis: To 5 mL of the *Sample solution* add 5 mL of sodium hydroxide TS. Boil for a few min, cool, and acidify with 3 N hydrochloric acid.
  Acceptance criteria: The solution is strongly opalescent.
- **B.**
  Sample solution: 1 in 20, in water
  Analysis: To 2 mL of the *Sample solution* add 0.5 mL of bromine TS, dropwise.
  Acceptance criteria: The bromine is not decolorized (distinction from polysorbate 80).
- **C.** A mixture of 60 volumes of Polysorbate 60 and 40 volumes of water yields a gelatinous mass at normal and lower than normal room temperatures.

IMPURITIES

- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.25%
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 ppm

SPECIFIC TESTS

- **ACID VALUE**
  Sample: 10.0 of Polysorbate 60
  Analysis: Transfer the *Sample* to a wide-mouth, 250-mL conical flask, and add 50 mL of neutralized alcohol. Heat on a steam bath nearly to boiling, shaking thoroughly occasionally while heating. Invert a beaker over the mouth of the flask, cool under running water, and add 5 drops of phenolphthalein TS. Titrate with 0.1 N sodium hydroxide VS.
  Acceptance criteria: NMT 4 mL of 0.1 N sodium hydroxide, corresponding to an acid value of 2.2
- **FATS AND FIXED OILS,** *Hydroxyl Value* ⟨**401**⟩**:** 81–96
- **FATS AND FIXED OILS,** *Saponification Value* ⟨**401**⟩**:** 45–55
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 3.0%

ADDITIONAL REQUIREMENTS

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

Polysorbate 80

Attributes	EP	JP	USP
Definition	+	+	+
Identification (Composition of Fatty Acids)	+	+	+
Acid Value	+	+	+
Hydroxyl Value	+	+	+
Peroxide Value	+	+	+
Saponification Value	+	+	+
Composition of Fatty Acids	+	+	+
Ethylene Oxide and Dioxane	+	+	+
Water	+	+	+
Residue on Ignition	+	+	+
Storage	+	+	+

Legend: + will adopt and implement; – will not stipulate
Nonharmonized attributes: Characters, Identification by IR (EP), Heavy Metals (USP)
Each pharmacopeia will adapt the text to take account of local reference substances and spectra and reagent specifications.

Sorbitan, mono-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs., (*Z*)-;
Polyoxyethylene 20 sorbitan monooleate [9005-65-6].

DEFINITION

Polysorbate 80 is a mixture of partial esters of fatty acids, mainly oleic acid, with sorbitol and its anhydrides ethoxylated with approximately 20 moles of ethylene oxide for each mole of sorbitol and sorbitol anhydrides.

IDENTIFICATION

- It complies with the test for *Composition of Fatty Acids*.

ASSAY

- **COMPOSITION OF FATTY ACIDS**
  Diluent: 20 g/L of sodium hydroxide in methanol
  Saturated sodium chloride solution: Sodium chloride and water (1:2). Before use, decant the solution from any undissolved substance and filter, if necessary.
  Reference solution A: Prepare 0.50 g of the mixture of calibrating substances with the composition described in *Table 1*. Dissolve in heptane, and dilute with heptane to 50.0 mL.
  Reference solution B: *Reference solution A* in heptane (1 in 10)
  Reference solution C: Prepare 0.50 g of a mixture of fatty acid methyl esters, which corresponds to the composition of the substance to be examined. Dissolve in heptane, and dilute with heptane to 50.0 mL. [NOTE—Commercially available mixtures of fatty acid methyl esters may also be used.]
  Sample solution: Dissolve 0.10 g of Polysorbate 80 in 2 mL of *Diluent* in a 25-mL conical flask, and boil under a reflux condenser for 30 min. Add 2.0 mL of 14% boron trifluoride–methanol through the condenser, and boil for 30 min. Add 4 mL of heptane through the condenser, and boil for 5 min. Cool and add 10.0 mL of *Saturated sodium chloride solution*, shake for about 15 s, and add a quantity of *Saturated sodium chloride solution* such that the upper phase is brought into the neck of the flask. Collect 2 mL of the upper phase, wash with three quantities, each of 2 mL, of water, and dry over anhydrous sodium sulfate.