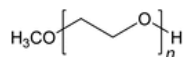


Status: Currently Official on 16-Feb-2025
 Official Date: Official as of 01-Jan-2018
 Document Type: NF Monographs
 DocId: GUID-E16D3B2E-ECDC-4C78-B276-276F7697DFB5_3_en-US
 DOI: https://doi.org/10.31003/USPNF_M66475_03_01
 DOI Ref: 147sk

© 2025 USPC
 Do not distribute

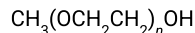
Polyethylene Glycol Monomethyl Ether



Poly(oxy-1,2-ethanediyl), α -methyl- ω -hydroxy-;
 Methoxy polyethylene glycol
 CAS RN[®]: 9004-74-4.

DEFINITION

Polyethylene Glycol Monomethyl Ether is an addition polymer of ethylene oxide and methanol, represented as:



in which n represents the average number of oxyethylene groups. The average molecular weight is NLT 95.0% and NMT 105.0% of the labeled nominal value if the labeled nominal value is below 1000; it is NLT 90.0% and NMT 110.0% of the labeled nominal value if the labeled nominal value is between 1000 and 4750; and it is NLT 87.5% and NMT 112.5% of the labeled nominal value if the labeled nominal value is above 4750.

ASSAY

• AVERAGE MOLECULAR WEIGHT

Phthalic anhydride solution: Place 49.0 g of phthalic anhydride into an amber bottle, and dissolve in 300 mL of pyridine, either from a freshly opened bottle or freshly distilled over phthalic anhydride. Shake vigorously until completely dissolved. Add 7 g of imidazole, swirl carefully to dissolve, and allow to stand for 16 h before using.

Sample solution for liquid Polyethylene Glycol Monomethyl Ethers: Carefully introduce 25.0 mL of the *Phthalic anhydride solution* into a dry, heat-resistant pressure bottle. Add a weighed amount of the sample, equivalent to its expected average molecular weight divided by 80. Insert the stopper in the bottle, and wrap it securely in a cloth bag.

Sample solution for solid Polyethylene Glycol Monomethyl Ethers: Carefully introduce 25.0 mL of *Phthalic anhydride solution* into a dry, heat-resistant pressure bottle. Add an amount of the sample, equivalent to its expected molecular weight divided by 80; however, because of limited solubility, do not use more than 25 g. Add 25 mL of pyridine, either from a freshly opened bottle or freshly distilled over phthalic anhydride, swirl to dissolve, insert the stopper in the bottle, and wrap it securely in a cloth bag.

Analysis: Immerse the bottle in a water bath maintained at 96°–100° to the same depth as that of the mixture in the bottle. Remove the bottle from the bath after 5 min, and without unwrapping, swirl for 30 s to homogenize. Heat in the water bath for 30 min (60 min for Polyethylene Glycol Monomethyl Ethers having molecular weights of 3000 or higher), then remove from the bath, and allow to cool to room temperature. Uncap the bottle carefully to release any pressure, remove from the bag, add 10 mL of water, and swirl thoroughly. Wait for 2 min, add 0.5 mL of a solution of phenolphthalein in pyridine (1 in 100). Titrate with 0.5 N sodium hydroxide VS to the first pink color that persists for 15 s, recording the volume, in mL, of 0.5 N sodium hydroxide required as V_s . Perform a blank determination on 25.0 mL of *Phthalic anhydride solution* plus any additional pyridine added to the bottle, and record the volume, in mL, of 0.5 N sodium hydroxide required as V_b . Calculate the average molecular weight:

$$\text{Result} = (1000 \times W) / [(V_b - V_s) \times N]$$

W = weight of Polyethylene Glycol Monomethyl Ether taken for the *Sample solution* (g)

V_b = volume of 0.5 N sodium hydroxide consumed by the blank (mL)

V_s = volume of 0.5 N sodium hydroxide consumed by the sample (mL)

N = normality of the sodium hydroxide solution

Acceptance criteria: See [Table 1](#).

Table 1

Label Claim (nominal value)	Acceptance Criteria (%)
<1000	95.0–105.0
1000–4750	90.0–110.0
>4750	87.5–112.5

IMPURITIES

• **RESIDUE ON IGNITION (281)**

Sample: 25 g of Polyethylene Glycol Monomethyl Ether, moistened with 2 mL of sulfuric acid in a platinum dish

Acceptance criteria: NMT 0.1%

• **LIMIT OF ETHYLENE GLYCOL AND DIETHYLENE GLYCOL** (for Polyethylene Glycol Monomethyl Ether having a nominal molecular weight of less than 600)

Standard solution: 500 µg/mL of ethylene glycol and 500 µg/mL of diethylene glycol in water

Sample solution: 400 mg/mL of Polyethylene Glycol Monomethyl Ether in water

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: GC

Detector: Flame ionization

Column: 3-mm × 1.0-m; 60- to 80-mesh support S2

Temperatures

Column: 200°

Injection port: 260°

Carrier gas: Nitrogen or another suitable inert gas

Flow rate: 20 mL/min

Injection volume: 1.0 µL

Analysis

Samples: *Standard solution* and *Sample solution*

[NOTE—The elution order is ethylene glycol, diethylene glycol, and polyethylene glycol monomethyl ether.]

Calculate the percentage of ethylene glycol and diethylene glycol in the portion of Polyethylene Glycol Monomethyl Ether taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak height of ethylene glycol or diethylene glycol from the *Sample solution*

r_S = peak height of ethylene glycol or diethylene glycol from the *Standard solution*

C_S = concentration of ethylene glycol or diethylene glycol in the *Standard solution*

C_U = concentration of Polyethylene Glycol Monomethyl Ether in the *Sample solution*

Acceptance criteria: NMT 0.25% of combined ethylene glycol and diethylene glycol

• **LIMIT OF ETHYLENE GLYCOL AND DIETHYLENE GLYCOL** (for Polyethylene Glycol Monomethyl Ether having a nominal molecular weight of 600–1500)

Solution A: 62.5 mg/mL of ceric ammonium nitrate in 0.25 N nitric acid. Use within 3 days.

Solution B: Freshly distilled acetonitrile and water (50:50)

Standard solution: 2.5 mg/mL of diethylene glycol in *Solution B*

Sample solution: Dissolve 50.0 g of Polyethylene Glycol Monomethyl Ether in 75 mL of diphenyl ether, previously warmed if necessary, to melt the crystals, in a 250-mL distilling flask. Slowly distill at a pressure of 1–2 mm of mercury into a receiver graduated to 100 mL in 1-mL subdivisions until 25 mL of distillate has been collected. Add 20.0 mL of water to the distillate, shake vigorously, and allow the layers to separate. Cool in an ice bath to solidify the diphenyl ether and facilitate its removal. Filter the separated aqueous layer, wash the diphenyl ether with 5.0 mL of ice-cold water, pass the washings through the filter, and collect the filtrate and washings in a 25-mL volumetric flask.