⟨469⟩ ETHYLENE GLYCOL, DIETHYLENE GLYCOL, AND TRIETHYLENE GLYCOL IN ETHOXYLATED SUBSTANCES

The following procedure is used to determine the concentration of residual ethylene glycol, diethylene glycol, and triethylene glycol in ethoxylated products. Ethoxylated products may contain residual ethylene glycol, diethylene glycol, and triethylene glycol as a result of the manufacturing process. The procedure is suitable for the following substances:

1. Polyethylene glycol 200
2. Polyethylene glycol 300
3. Polyethylene glycol 400
4. Polyethylene glycol 600
5. Polyethylene glycol 1000
6. Polysorbate 20
7. Polysorbate 40
8. Polysorbate 60
9. Polysorbate 80
10. Polyethylene glycol monomethyl ether 350
11. Polyethylene glycol monomethyl ether 550
12. Polyoxyl 35 castor oil
13. Polyoxyl 15 hydroxystearate
14. Polyoxyl 20 cetostearyl ether
15. Polyoxyl 8 stearate
16. Octoxynol 9
17. Nonoxynol 9

IMPURITIES

• **PROCEDURE**

Diluent: Acetone

Standard solution: 25 µg/mL of USP Ethylene Glycol RS, 40 µg/mL of USP Diethylene Glycol RS, 40 µg/mL of USP Triethylene Glycol RS, and 40 µg/mL of USP Butane-1,3-diol RS (internal standard) in *Diluent*

Sample solution: 40 mg/mL of the test substance and 40 µg/mL of USP Butane-1,3-diol RS (internal standard) in *Diluent*

Chromatographic system

(See *Chromatography* ⟨621⟩*, System Suitability*.)

Mode: GC

Detector: Flame ionization

Column: 0.53-mm × 30-m capillary column bonded with a 1.0-µm layer of phase G3

Temperatures

Detector: 290°

Injection port: 270°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	10	60	5
60	10	170	0
170	15	280	0, 60[a]

[a] Hold time was 0 min for the *Standard solution* and 60 min for the *Sample solution* and *Diluent*.

Carrier gas: Helium

Flow rate: 5.0 mL/min

Injection volume: 1.0 µL

Injection type: Split injection, split ratio is 2:1

Liner: General-purpose split/splitless, tapered, glass wool, deactivated

Run time: 26 min for the *Standard solution*; 86 min for the *Sample solution* and *Diluent*

System suitability

Sample: *Standard solution*

[NOTE—See *Table 2* for the relative retention times.]

Table 2

Name	Relative Retention Time
Ethylene glycol	0.45
Butane-1,3-diol (internal standard)	1.00
Diethylene glycol	1.25
Triethylene glycol	1.70

System suitability requirements

Resolution: NLT 20 between ethylene glycol and butane-1,3-diol; NLT 20 between butane-1,3-diol and diethylene glycol; NLT 20 between diethylene glycol and triethylene glycol

Tailing factor: 0.8–1.8 for each of the four peaks assigned to ethylene glycol, butane-1,3-diol, diethylene glycol, and triethylene glycol

Relative standard deviation: NMT 5.0% for the peak response ratio of the respective glycol (ethylene glycol, diethylene glycol, or triethylene glycol) to the internal standard

Analysis

Samples: *Standard solution* and *Sample solution*

Identify the ethylene glycol, diethylene glycol, and triethylene glycol peaks in the *Sample solution* by comparison with those in the *Standard solution*.

Calculate the content of ethylene glycol, diethylene glycol, or triethylene glycol, in µg/g, in the portion of test substance taken:

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

R_U = peak response ratio of the respective glycol to the internal standard (peak response of the respective glycol/peak response of the internal standard) from the *Sample solution*

R_S = peak response ratio of the respective glycol to the internal standard (peak response of the respective glycol/peak response of the internal standard) from the *Standard solution*

C_S = concentration of the respective glycol (ethylene glycol, diethylene glycol, or triethylene glycol) in the *Standard solution* (µg/mL)

C_U = concentration of the test substance in the *Sample solution* (mg/mL)

F = conversion factor (1000 mg/g)

ADDITIONAL REQUIREMENTS

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Butane-1,3-diol RS
USP Diethylene Glycol RS
USP Ethylene Glycol RS
USP Triethylene Glycol RS