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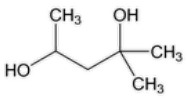
Hexylene Glycol

Change to read:



$C_6H_{14}O_2$ ▲118.18▲ (NF 1-May-2020)

2,4-Pentanediol, 2-methyl-;

2-Methyl-2,4-pentanediol;

▲2-Methylpentane-2,4-diol▲ (NF 1-May-2020) CAS RN®: 107-41-5.

DEFINITION

Change to read:

Hexylene Glycol ▲contains NLT 98.0% and NMT 102.0% of 2-methylpentane-2,4-diol, calculated on the anhydrous basis.▲ (NF 1-May-2020)

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197F**▲ (CN 1-May-2020)

Sample: Undried specimen

Acceptance criteria: Meets the requirements

Add the following:

▲• **B. Chromatographic Identity**

Analysis: Examine the chromatograms from the *Assay*.

Acceptance criteria: The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*.▲ (NF 1-May-2020)

ASSAY

Add the following:

▲• **Procedure**

Diluent: Methanol

Internal standard solution: 1.0 mg/mL of USP Propylene Glycol RS (internal standard) in *Diluent*

System suitability solution: 0.1 mg/mL of diacetone alcohol and 1.0 mg/mL of USP Hexylene Glycol RS in *Internal standard solution*

Standard solution: 1.0 mg/mL of USP Hexylene Glycol RS in *Internal standard solution*

Sample solution: 1.0 mg/mL of Hexylene Glycol in *Internal standard solution*

Chromatographic system

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

Mode: GC

Detector: Flame ionization

Column: 0.32-mm × 60-m capillary; bonded with a 1.0-µm layer of phase G1

Temperatures

Injection port: 200°

Detector: 300°

Column: See *Table 1*.

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
40	0	40	3
40	15	200	15

Carrier gas: Helium

Pressure: 15 psi (constant pressure mode)

Injection volume: 1.0 µL

Injection type: Split ratio, 100:1

Liner: Ultra inert liner with glass wool, low pressure drop[1]

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The approximate relative retention times are listed in *Table 2*.]

Suitability requirements

Resolution: NLT 5 between hexylene glycol and diacetone alcohol, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 2.0% for the peak response ratio of hexylene glycol to the internal standard, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of hexylene glycol in the portion of the sample taken:

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

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

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

C_S = concentration of USP Hexylene Glycol RS in the *Standard solution* (mg/mL)

C_U = concentration of Hexylene Glycol in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis▲ (NF 1-May-2020)

IMPURITIES

Change to read:

• **▲ORGANIC IMPURITIES**

Diluent and **Chromatographic system:** Proceed as directed in the *Assay*.

Sensitivity solution: 0.01 mg/mL of USP Hexylene Glycol RS in *Diluent*

System suitability solution: 0.2 mg/mL of USP Acetone RS and 0.2 mg/mL of USP 2-Propanol RS in *Diluent*

Standard solution: 0.02 mg/mL of USP Hexylene Glycol RS in *Diluent*

Sample solution: 20.0 mg/mL of Hexylene Glycol in *Diluent*

System suitability

Samples: *Sensitivity solution, System suitability solution*, and *Standard solution*

[NOTE—The approximate relative retention times are listed in *Table 2*.]

Suitability requirements

Resolution: NLT 1.5 between the acetone peak and the 2-propanol peak, *System suitability solution*

Relative standard deviation: NMT 5.0%, determined from the hexylene glycol peak, *Standard solution*

Signal-to-noise ratio: NLT 10, determined from the hexylene glycol peak, *Sensitivity solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each individual impurity in the portion of the sample taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak area of each individual impurity from the *Sample solution*

r_S = peak area of hexylene glycol from the *Standard solution*

C_S = concentration of USP Hexylene Glycol RS in the *Standard solution* (mg/mL)

C_U = concentration of Hexylene Glycol in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Acetone	0.42	0.9	0.1
2-Propanol	0.43	0.9	0.1
4-Methylpentan-2-one	0.77	1.3	0.1
4-Methylpentan-2-ol	0.81	1.4	0.1
Diacetone alcohol[a]	0.91	1.0	0.1
Hexylene glycol	1.0	—	—
Any other individual impurity	—	▲1.0▲ (ERR 1-May-2020)	0.1
Total impurities	—	—	1.0▲ (NF 1-May-2020)

[a] 4-Hydroxy-4-methylpentan-2-one.

SPECIFIC TESTS

- **Specific Gravity ⟨841⟩:** 0.917–0.923
- **Refractive Index ⟨831⟩:** 1.424–1.430
- **Acidity**

  Sample: 10 mL

  Analysis: Mix 1 mL of phenolphthalein TS with 50 mL of water, and add 0.1 N sodium hydroxide until the solution remains pink for 30 s. Add the *Sample*, and titrate with 0.10 N sodium hydroxide until the original pink color returns and remains for 30 s.

  Acceptance criteria: NMT 0.20 mL of 0.10 N sodium hydroxide is required.
- **Water Determination ⟨921⟩, *Method I* :** NMT 0.5%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers.

Change to read:

- **USP Reference Standards ⟨11⟩**

▲ USP Acetone RS▲ (NF 1-May-2020)

USP Hexylene Glycol RS

▲ USP 2-Propanol RS

USP Propylene Glycol RS▲ (NF 1-May-2020)

[1] Agilent PN 5190-3165 liner has been suitable. Other equivalent liners are also suitable.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
HEXYLENE GLYCOL	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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