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Azeotropic Isopropyl Alcohol

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DEFINITION
Azeotropic Isopropyl Alcohol contains NLT 91.0% and NMT 93.0% of isopropyl alcohol, by volume, the remainder consisting of water.

IDENTIFICATION

- **A. INFRARED ABSORPTION:** The IR absorption spectrum of a thin film of it exhibits a strong broad band at 3.0 μm; a strong region of absorption between 3.35 and 3.5 μm, with its highest peak at 3.36 μm, and others at 3.41 and 3.47 μm; many weak peaks between 3.6 and 6.0 μm, among the most noticeable being those at 3.68, 3.77, 3.97, 4.17, and 5.26 μm; a broad band at 6.2 μm; a strong region of absorption between 6.7 and 7.8 μm, the most prominent features being the peaks at 6.80, 7.09, 7.25 (the highest), 7.46, and 7.63 μm; a strong region of absorption between 8.5 and 9.2 μm, peaking at 8.6, 8.85, and 9.0 μm; and strong peaks at 10.5 and 12.3 μm.

Add the following:

▲ **B. LIMIT OF METHANOL**

[NOTE—This test must be performed to be in compliance with USP, in addition to *Identification A* above.]

System suitability solution, Sample solution, Standard solution A, Chromatographic system, and System suitability: Proceed as directed in the *Volatile Impurities* test.

Analysis: Proceed as directed in the *Volatile Impurities* test, *Methanol calculation*.

Acceptance criteria: Meets the requirements in [Table 3](#) for methanol▲ (RB 1-Feb-2022)

IMPURITIES

• **LIMIT OF NONVOLATILE RESIDUE**

Sample: 50 mL

Analysis: Evaporate the *Sample* in a tared porcelain dish on a steam bath to dryness, and heat at 105° for 1 h.

Acceptance criteria: The weight of the residue does not exceed 2.5 mg (0.005%).

Change to read:

• **VOLATILE IMPURITIES**

System suitability solution: ▲200 μL/L of methanol and 1000 μL/L of ethyl acetate in▲ (RB 1-Feb-2022) [USP 2-Propanol System Suitability RS](#)

Sample solution: Azeotropic Isopropyl Alcohol ▲(Substance under test)

Standard solution A: 200 μL/L of methanol in *Sample solution*

[NOTE—To be performed as a part of *Identification B*.]

Standard solution B: 1000 μL/L each of acetone, diisopropyl ether, ethyl ether, 1-propanol, 2-butanol, and ethyl acetate in *Sample solution*▲ (RB 1-Feb-2022)

Chromatographic system

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

Mode: GC

Detector: ▲Flame ionization▲ (RB 1-Feb-2022)

Column: 0.25-mm × 60-m, coated with a 1.4-μm film of phase G43

Temperature

Injector: 150°

Detector: 200°

Column: See [Table 1](#).

Table 1

Initial Temperature (°)	Temperature Ramp (°/min)	Final Temperature (°)	Hold Time at Final Temperature (min)
35	▲ (RB 1-Feb-2022)	35	5
35	1	45	▲ (RB 1-Feb-2022)
45	10	100	▲5▲ (RB 1-Feb-2022)

Carrier gas: Helium

▲Flow rate: 2.3 mL/min▲ (RB 1-Feb-2022)

Injection ▲volume:▲ (RB 1-Feb-2022) 1 µL

▲Injection type: Split injection; split ratio is about 50:1. [NOTE—A 4-mm straight liner is suitable.]▲ (RB 1-Feb-2022)

Run time: ▲26▲ (RB 1-Feb-2022) min

System suitability

Sample: System suitability solution

▲[NOTE—See [Table 2](#).]

Table 2

Name	Relative Retention Time
Methanol	0.5
Ethyl ether	0.8
Acetone	0.9
Isopropyl alcohol	1.0
Diisopropyl ether	1.3
n-Propyl alcohol (1-propanol)	1.4
Ethyl acetate ^a	1.6
2-Butanol	1.7▲ (RB 1-Feb-2022)

^a Ethyl acetate Reference Standard is not a known impurity. It is used for the calculation of unspecified impurities only.

Suitability requirements

Resolution: NLT 1.5 between acetone and isopropyl alcohol

Signal-to-noise ratio: NLT 10 for any of the following peaks: ▲methanol,▲ (RB 1-Feb-2022) ethyl ether, acetone, isopropyl alcohol, diisopropyl ether, 1-propanol, 2-butanol, ▲and ethyl acetate.▲ (RB 1-Feb-2022)

Tailing factor: NMT 2.0 for the isopropyl alcohol peak

Relative standard deviation: NMT 2.0% for the isopropyl alcohol peak ▲of 6 replicate injections of System suitability solution▲ (RB 1-Feb-2022)

Analysis

Samples: Sample solution, ▲Standard solution A, and Standard solution B

Methanol calculation

[NOTE—To be performed as a part of Identification B.]

$$\text{Result (\% v/v)} = \{[M_U / (M_S - M_U)] \times C_M\} / 10,000$$

M_U = peak area of methanol in the *Sample solution*

M_S = peak area of methanol in *Standard solution A*

C_M = concentration of spiked methanol in *Standard solution A* (μL/L)

Individual known impurity (ethyl ether, acetone, diisopropyl ether, 1-propanol, 2-butanol) calculation

$$\text{Result (\% v/v)} = \{[K_U/(K_S - K_U)] \times C_K\}/10,000$$

K_U = peak area of individual known impurity in the *Sample solution*

K_S = peak area of individual known impurity in *Standard solution B*

C_K = concentration of spiked individual known impurity in *Standard solution B* (μL/L)

Individual unspecified impurity calculation

$$\text{Result (\% v/v)} = [(r_U/r_S) \times C_S]/10,000$$

r_U = peak area of each unspecified impurity in the *Sample solution*

r_S = peak area of ethyl acetate in *Standard solution B*

C_S = concentration of ethyl acetate in *Standard solution B* (μL/L)▲ (RB 1-Feb-2022)

Acceptance criteria: ▲See [Table 3](#).

Table 3

Impurity	Percentage (% v/v)
Methanol ^a	NMT 0.02 ^a
Each other individual known impurity (ethyl ether, acetone, diisopropyl ether, 1-propanol, 2-butanol)	NMT 0.1
Individual unspecified impurity	NMT 0.1
Total impurities	NMT 1.0▲ (RB 1-Feb-2022)

^a To be performed as a part of *Identification B*.

SPECIFIC TESTS

• **SPECIFIC GRAVITY (841):** 0.815–0.810, indicating 91.0%–93.0% of isopropyl alcohol (C₃H₈O) by volume

• **REFRACTIVE INDEX (831):** 1.376–1.378 at 20°

• ACIDITY

Sample: 50 mL

Analysis: Place the *Sample* in a suitable flask, and add 100 mL of carbon dioxide-free water. Add 2 drops of phenolphthalein TS, and titrate with 0.020 N sodium hydroxide to a pink color that persists for 30 s.

Acceptance criteria: NMT 0.70 mL of 0.020 N sodium hydroxide is required for neutralization.

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Preserve in tight containers, remote from heat.

• **USP REFERENCE STANDARDS (11).**

[USP 2-Propanol System Suitability RS](#)

It is a mixture of the following: ethyl ether (0.1%), acetone (0.1%), diisopropyl ether (0.1%), 1-propanol (0.1%), 2-butanol (0.1%), and isopropyl alcohol (99.5%).

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
AZEOTROPIC ISOPROPYL ALCOHOL	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

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