Menthol

Type of Posting	Revision Bulletin
Posting Date	29–May–2015; updated 01–Jun–2015*
Official Date	01–Jun–2015
Expert Committee	Monographs—Dietary Supplements and Herbal Medicines
Reason for Revision	Compliance

In accordance with the Rules and Procedures of the 2010-2015 Council of Experts, the Monographs—Dietary Supplements and Herbal Medicines Expert Committee has revised Menthol monograph.

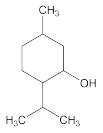
Comments and data received show that menthol obtained from natural sources does not meet the current limit of 0.1% for Individual impurities; therefore the Expert Committee has decided to increase the limit for Individual impurities to 0.3% based on the data submitted to USP.

The Menthol Revision Bulletin supersedes the currently official monograph. The Revision Bulletin will be incorporated in the *USP 39–NF 34*.

Should you have any questions, please contact Nam-Cheol Kim, Scientific Liaison (301–230–7428 or nck@usp.org).

* The Revision Bulletin Notice was updated on June 1, 2015, to correct the official date for the Revision Bulletin listed in the notice. The original posting on May 29, 2015 had the incorrect official date of July 1, 2015 listed on the Notice instead of June 1, 2015. The monograph that was posted on May 29, 2015 had the correct official date of June 1, 2015 and no changes were made to the text of the monograph.

Menthol



$C_{10}H_{20}O$ 156.27
Cyclohexanol, 5-methyl-2-(1-methylethyl)- [1490-04-6].

DEFINITION
Menthol is an alcohol obtained from oils derived from a variety of mints or prepared synthetically. Menthol may be levorotatory (*l*-menthol) from natural or synthetic sources, or racemic (*dl*-menthol). It contains NLT 98.0% and NMT 102.0% of menthol ($C_{10}H_{20}O$).

IDENTIFICATION
- **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the menthol peak of the *Standard solution*, as obtained in the *Assay*.
- **B.** It meets the requirements in *Specific Tests* for *Optical Rotation* ⟨781S⟩, *Specific Rotation*.

ASSAY
- **PROCEDURE**

Internal standard solution: 0.5 mg/mL of anethole in hexanes
Standard solution: 0.5 mg/mL of USP Menthol RS in *Internal standard solution*
Sample solution: 0.5 mg/mL of Menthol in *Internal standard solution*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: GC
Detector: Flame ionization
Column: 0.53-mm × 30-m fused silica; coated with a 1-µm layer of G16 stationary phase
Temperatures
Injection port: 250°
Detector: 250°
Column: 130° (isothermal)
Carrier gas: Helium
Flow rate: 10 mL/min
Injection volume: 1 µL
Injection type: Split ratio of 10:1
System suitability
Sample: *Standard solution*
[NOTE—The relative retention times for menthol and anethole are about 0.5 and 1.0, respectively.]
Suitability requirements
Tailing factor: NMT 2.0 for the menthol peak
Relative standard deviation: NMT 2.0% for the peak response ratio of menthol to anethole in replicate injections
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of menthol ($C_{10}H_{20}O$) in the portion of Menthol taken:

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

R_U = peak response ratio of menthol to anethole from the *Sample solution*
R_S = peak response ratio of menthol to anethole from the *Standard solution*
C_S = concentration of USP Menthol RS in the *Standard solution* (mg/mL)
C_U = concentration of Menthol in the *Sample solution* (mg/mL)
Acceptance criteria: 98.0%–102.0%

IMPURITIES
- **LIMIT OF NONVOLATILE RESIDUE**

Analysis: Evaporate 2 g, accurately weighed, in a tared open porcelain dish on a steam bath, and dry the residue at 105° for 1 h.
Acceptance criteria: NMT 0.05%

Change to read:

- **RELATED COMPOUNDS**

Internal standard solution, Standard solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Sample solution: 5 mg/mL of Menthol in hexanes
Analysis
Sample: *Sample solution*
Calculate the percentage of each individual impurity in the portion of Menthol taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each impurity from the *Sample solution*
r_T = sum of the responses of all the peaks from the *Sample solution*
Acceptance criteria
Individual impurities: •NMT 0.3%• (RB 1-Jun-2015)
Total impurities: NMT 2.0%

- **READILY OXIDIZABLE SUBSTANCES IN *dl*-MENTHOL**

Sample solution: Place 500 mg of *dl*-menthol in a clean, dry test tube, and add 10 mL of a solution of potassium permanganate, prepared by diluting 3 mL of 0.1 N potassium permanganate with water to 100 mL.
Analysis: Place the test tube in a beaker with water at a temperature between 45° and 50°. Remove the tube from the bath at intervals of 30 s, and mix quickly by shaking.
Acceptance criteria: The purple color of potassium permanganate is still apparent after 5 min.

SPECIFIC TESTS
- **CONGEALING RANGE OF *dl*-MENTHOL**

(See *Congealing Temperature* ⟨651⟩.)
[NOTE—Perform this test preferably in a room having a temperature below 30° and a relative humidity below 50%.]
Sample: 10 g of *dl*-menthol, previously dried in a desiccator over silica gel for 24 h
Analysis: Place the *Sample* in a dry test tube having an internal diameter of 18–20 mm, and melt the contents at a temperature of about 40°. Suspend the test tube in water having a temperature of 23°–25°, and stir the contents of the tube continually with a thermometer, keeping the bulb of the thermometer immersed in the liquid.
Acceptance criteria: *dl*-Menthol congeals at a temperature between 27° and 28°. Shortly after the temperature has stabilized at the congealing point, add a few mg of dried *dl*-menthol to the congealed mass, and continue stirring. After a few min, the temperature of the mass quickly rises to 30.5°–32.0°.

- **MELTING RANGE OF *l*-MENTHOL**

(See *Melting Range or Temperature* ⟨741⟩.)

Acceptance criteria: 41°–44°

- **OPTICAL ROTATION** ⟨**781S**⟩**,** *Specific Rotation*
  Sample solution: 100 mg/mL in alcohol
  Acceptance criteria
  ***l*-Menthol:** –45° to –51°
  ***dl*-Menthol:** –2° to +2°

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers, preferably at controlled room temperature.
- **LABELING:** Label it to indicate whether it is levorotatory or racemic.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Menthol RS