Saccharin

Add the following:

• Portions of this monograph that are national USP text, and are not part of the harmonized text, are marked with symbols (**) to specify this fact. See (NF32)

C₇H₅NO₃S  183.18
1,2-Benzisothiazol-3(2H)-one, 1,1-dioxide;
1,2-Benzisothiazolin-3-one, 1,1-dioxide [81-07-2].

DEFINITION
Saccharin contains NLT 99.0% and NMT 101.0% of saccharin (C₇H₅NO₃S), calculated on the dried basis.

IDENTIFICATION
• A. INFRARED ABSORPTION (197K)

ASSAY
• PROCEDURE
Sample:  500 mg
Analysis:  Dissolve the Sample in 40 mL of alcohol. Add 40 mL of water and phenolphthalein TS. Titrate with 0.1 N sodium hydroxide. Perform a blank titration, if necessary, and make the appropriate correction. Each mL of 0.1 N sodium hydroxide is equivalent to 18.32 mg of saccharin (C₇H₅NO₃S).
Acceptance criteria:  99.0%–101.0% on the dried basis

IMPURITIES
• RESIDUE ON IGNITION (281):  NMT 0.2%, using an ignition temperature of 600 ± 50°

Change to read:

• **(NF32) HEAVY METALS, Method II (231):  NMT 10 ppm** See (NF32)

Change to read:

• **(NF32) LIMIT OF TOLUENESULFONAMIDES**
Internal standard solution:  0.25 mg/mL of caffeine in methylene chloride
Standard stock solution:  20.0 µg/mL of USP o-Toluenesulfonamide RS and 20.0 µg/mL of USP p-Toluenesulfonamide RS in methylene chloride
Standard solution:  Evaporate 5.0 mL of the Standard stock solution to dryness in a stream of nitrogen. Dissolve the residue in 1 mL of the Internal standard solution.
Sample solution:  Suspend 10 g of Saccharin in 20 mL of water, and dissolve using 5–6 mL of 10 N sodium hydroxide. If necessary, adjust the solution with 1 N sodium hydroxide or 1 N hydrochloric acid to a pH of 7–8, and dilute with water to 50 mL. Shake the solution with four quantities each of 50 mL of methylene chloride. Combine the lower layers, dry over anhydrous sodium sulfate, and filter. Wash the filter and the sodium sulfate with 10 mL of methylene chloride. Combine the solution and the washings, and evaporate almost to dryness in a water bath at a temperature not exceeding 40°. Using a small quantity of methylene chloride, quantitatively transfer the residue into a suitable 10-mL tube, evaporate to dryness in a stream of nitrogen, and dissolve the residue in 1.0 mL of the Internal standard solution.
Blank solution:  Evaporate 200 mL of methylene chloride to dryness in a water bath at a temperature not exceeding 40°. Dissolve the residue in 1 mL of methylene chloride.

Chromatographic system
(See Chromatography (621), System Suitability.)
Mode:  GC
Detector:  Flame ionization
Column:  0.53-mm × 10-m fused silica; coated with a 2-µm film of phase G3
Temperature
Injector:  250°
Detector:  250°
Column:  180°
Carrier gas:  Nitrogen
Flow rate:  10 mL/min
Injection volume:  1 µL
Split ratio:  2:1
System suitability
Samples:  Standard solution and Blank solution
[NOTE—The substances are eluted in the following order:  o-toluenesulfonamide, p-toluenesulfonamide, and caffeine.]
Suitability requirements:  No peaks at the retention times for the internal standard, o-toluenesulfonamide, or p-toluenesulfonamide; Blank solution
Resolution:  NLT 1.5 between o-toluenesulfonamide and p-toluenesulfonamide, Standard solution

Analysis
Samples:  Standard solution and Sample solution
Acceptance criteria:  See Table 1. If any peaks due to o-toluenesulfonamide and p-toluenesulfonamide appear in the chromatogram of the Sample solution, the ratio of their areas to that of the Internal standard solution is NMT the corresponding ratio in the chromatogram of the Standard solution.

Table 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Acceptance Criteria (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>o-Toluenesulfonamide</td>
<td>10</td>
</tr>
<tr>
<td>p-Toluenesulfonamide</td>
<td>10</td>
</tr>
</tbody>
</table>

• LIMIT OF BENZOATE AND SALICYLATE
Sample solution:  10 mL of a hot, saturated solution of saccharin
Analysis:  Add ferric chloride TS dropwise to the Sample solution.
Acceptance criteria:  No precipitate or violet color appears in the liquid.

SPECIFIC TESTS
• **(NF32) MELTING RANGE OR TEMPERATURE (741):  226°–230°** See (NF32)
• LOSS ON DRYING (731)
Analysis:  Dry at 105° for 2 h.
Acceptance criteria:  NMT 1.0%

READILY CARBONIZABLE SUBSTANCES TEST (271)
Sample solution:  40 mg/mL in sulfuric acid [94.5%–95.5% (w/w) of H₂SO₄]; maintained at 48°–50° for 10 min
Acceptance criteria:  The Sample solution has no more color than Matching Fluid A, when viewed against a white background.
Change to read:

- **CLARITY OF SOLUTION**

  [Note—The Sample solution is to be compared to Reference suspension A in diffused daylight 5 min after preparation of Reference suspension A.]

  Diluent: 200 g/L solution of sodium acetate

  Hydrazine solution: 10.0 mg/mL of hydrazine sulfate.

  Methenamine solution: Transfer 2.5 g of methenamine to a 100-mL glass-stoppered flask, add 25.0 mL of water, insert the glass stopper, and mix to dissolve.

  Primary opalescent suspension: Transfer 25.0 mL of Hydrazine solution to the Methenamine solution in the 100-mL glass-stoppered flask. Mix, and allow to stand for 24 h. [Note—This suspension should not be used beyond 24 h after preparation.]

  Reference suspension A: Opalescence standard and water (1 in 20)

  Reference suspension B: Opalescence standard and water (1 in 10)

  Sample solution: 200 mg/mL in Diluent A

  Analysis

  Samples: Diluent, Reference suspension A, Reference suspension B, Sample solution, and water

  Transfer a sufficient portion of the Sample solution to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of Reference suspension A, Reference suspension B, water, and Diluent to separate matching test tubes. Compare the solutions in diffused daylight, viewing vertically against a black background (see Spectrophotometry and Light-Scattering (851), Visual Comparison).

  [Note—The diffusion of light must be such that Reference suspension A can readily be distinguished from water, and that Reference suspension B can readily be distinguished from Reference suspension A.]

  Acceptance criteria: The Sample solution shows the same clarity as that of water or Diluent, or its opalescence is NMT that of Reference suspension A.

- **COLOR OF SOLUTION**

  Diluent A: 200-g/L solution of sodium acetate

  Diluent B: 10-g/L solution of hydrochloric acid

  Standard stock solution: Ferric chloride CS, cobaltous chloride CS, cupric sulfate CS, and Diluent B (3.0: 3.0: 2.4: 1.6)

  Standard solution: Standard stock solution and Diluent A

  Sample solution: Use the Sample solution from the test for Clarity of Solution.

  Analysis

  Samples: Diluent A, Standard solution, Sample solution, and water

  Transfer a sufficient portion of the Sample solution to a test tube of colorless, transparent, neutral glass with a flat base and an internal diameter of 15–25 mm to obtain a depth of 40 mm. Similarly transfer portions of the Standard solution, Diluent A, and water to separate, matching test tubes. Compare the solutions in diffused daylight, viewing vertically against a white background (see Spectrophotometry and Light-Scattering (851), Visual Comparison).

  Acceptance criteria: The Sample solution has the appearance of water or Diluent A, or is not more intensely colored than the Standard solution.

**ADDITIONAL REQUIREMENTS**

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at room temperature.

- **USP REFERENCE STANDARDS (11)**

  USP Saccharin RS
  USP o-Toluenesulfonamide RS
  USP p-Toluenesulfonamide RS