BRIEFING

Sodium Picosulfate. This monograph was posted on the USP Website as a draft USP Pending Monograph on September 28, 2007, and has been available for public comment for more than 90 days. The MD-GRE Expert Committee has reviewed all comments that were received and has approved the monograph as an Authorized USP Pending Monograph. The following is a summary of the comments received and the Expert Committee's responses.

Comment 1: It was proposed to add an IUPAC name for Sodium Picosulfate to the monograph.
Response 1: Comment incorporated. The IUPAC name is added as a second chemical name.
Comment 2: Under the test for *Color of Solution*, it was proposed to specify that carbon dioxide-free water is to be used.
Response 2: Comment incorporated.
Comment 3: Under *Organic Impurities*, several changes were proposed to make the monograph consistent with the version official in European Pharmacopeia 6.5:

- Change *Mobile phase* composition to acetonitrile and *Solution A* (45:55), and increase the column length to 25 cm
- Use *Mobile phase* as a *Diluent*
- Change the concentration of the *Sample solution* from 0.1 mg/mL to 0.5 mg/mL
- Add relative response factors to *Impurity Table 1*
- Add a *Diluted sample solution*, with a concentration of 0.5 µg/mL, to be injected along with the *Sample solution*, and revise the calculation, to take into account the concentration of *Diluted sample solution* and relative response factors
- Revise relative retention times and resolution requirement to reflect revised *Mobile phase* composition and column length

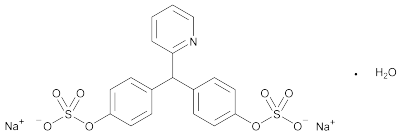
Response 3: Comment incorporated.

For the liquid chromatographic procedures in the test for *Organic Impurities*, Purospher RP 18 brand of L1 column was found suitable. The typical retention time for the sodium picosulfate peak is about 7.4 min.

(MD-GRE: E. Gonikberg.) RTS—C55188

Sodium Picosulfate

v. 1 Authorized September 1, 2009



$C_{18}H_{13}NNa_2O_8S_2 \cdot H_2O$ 499.42
4,4′-(2-Pyridylmethylene)diphenyl bis(hydrogen sulfate) disodium salt, monohydrate;
Disodium 4,4′-(pyridin-2-ylmethanediyl)dibenzenesulfonate 4,4′-(Pyridin-2-ylmethylene)bisphenyl bis (sodium sulfate), monohydrate;
Anhydrous 481.41
[10040-45-6].

DEFINITION

Sodium Picosulfate contains NLT 98.5% and NMT 100.5% of $C_{18}H_{13}NNa_2O_8S_2$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
- **B. IDENTIFICATION TESTS—GENERAL,** *Sodium* ⟨**191**⟩**:** Meets the requirements for the pyroantimonate precipitate test

ASSAY

- **PROCEDURE**

Sample solution: Dissolve 400 mg of Sodium Picosulfate in 80 mL of methanol.
Titrimetric system
(See *Titrimetry* ⟨541⟩.)
Mode: Direct titration
Titrant: 0.1 N Perchloric Acid VS
Endpoint detection: Potentiometric
Analysis
Sample: *Sample solution*
Calculate the percentage of $C_{18}H_{13}NNa_2O_8S_2$ in the portion of Sodium Picosulfate taken:

$$\text{Result} = [(V_S - V_B) \times N \times F/W] \times 100$$

V_S = volume of titrant used for sample (mL)
V_B = volume of titrant used for blank (mL)
N = titrant normality (mEq/mL)
F = 481.4 (mg/mEq)
W = sample weight (mg)

Acceptance criteria: 98.5%–100.5% on the anhydrous basis

IMPURITIES

Inorganic Impurities

- **CHLORIDE AND SULFATE,** *Chloride* ⟨**221**⟩**:** A 1.0-g portion shows no more chloride than corresponds to 0.30 mL of 0.020 N hydrochloric acid: NMT 0.02%.
- **CHLORIDE AND SULFATE,** *Sulfate* ⟨**221**⟩**:** A 500-mg portion shows no more sulfate than corresponds to 0.20 mL of 0.020 N sulfuric acid: NMT 0.04%.
- **HEAVY METALS,** *Method I* ⟨**231**⟩**:** NMT 10 ppm

Organic Impurities

- **PROCEDURE**

Solution A: 2.3 g/L of dibasic sodium phosphate dihydrate in water. For each L prepared add 200 mg of cetylrimethylammonium bromide and adjust with phosphoric acid to a pH of 7.5 prior to diluting to volume.
Mobile phase: Acetonitrile and *Solution A* (45:55)
Impurity solution: 0.25 mg/mL of USP Sodium Picosulfate Related Compound A RS in *Mobile phase*
System suitability solution: Transfer 2 mg of Sodium Picosulfate to a 100-mL volumetric flask, and dissolve in a small amount of water. Add 2.0 mL of the *Impurity solution,* dilute with water to volume, and mix.
Sample solution: 0.5 mg/mL of Sodium Picosulfate in *Mobile phase*
Diluted sample solution: 0.5 µg/mL of Sodium Picosulfate in *Mobile phase*, from *Sample solution*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 263 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Column temperature: 40°
Flow rate: 1 mL/min
Injection size: 40 µL
System suitability
Sample: *System suitability solution*
Suitability requirements
Resolution: NLT 4 between sodium picosulfate related compound A and sodium picosulfate
Analysis
Samples: *Sample solution* and *Diluted sample solution*
Calculate the percentage of each impurity in the portion of Sodium Picosulfate taken:

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

r_U = response for each impurity from the *Sample solution*
r_S = response for sodium picosulfate from the *Diluted sample solution*
C_S = concentration of sodium picosulfate in the *Diluted sample solution* (mg/mL)
C_U = concentration of Sodium Picosulfate in the *Sample solution* (mg/mL)
F = relative response factor (see *Impurity Table 1*)

Acceptance criteria
Individual impurities: See *Impurity Table 1*.
Total impurities: NMT 0.54%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
4,4′-[(Pyridin-2-yl)methylene]bisphenol	0.5	2.0	0.2
4-[(Pyridin-2-yl)(4-hydroxyphenyl)-methyl]phenyl sodium sulfate [a]	0.7	1.4	0.2
Sodium picosulfate	1.0	—	—
2,4′-[(Pyridin-2-yl)methylene]bisphenyl bis(sodium sulfate)	1.5	1.0	0.10
Any other individual impurity	—	1.0	0.10
Total impurities	—	—	0.5

[a] USP Sodium Picosulfate Related Compound A RS.

SPECIFIC TESTS

- **COLOR OF SOLUTION**
  Standard solution: Mix 0.75 mL of *Matching Fluid O* with 99.25 mL of dilute hydrochloric acid (10 g/1000 mL).
  Sample solution: Dissolve 2.5 g of Sodium Picosulfate in 50 mL of carbon dioxide-free water.
  [NOTE—Retain the remaining portion of the *Sample solution* for the test for *Acidity and Alkalinity*.]
  Analysis: Proceed as directed under *Color and Achromicity* ⟨631⟩.
  Acceptance criteria: The *Sample solution* is not more intensely colored than the *Standard solution.*
- **ACIDITY AND ALKALINITY**
  Analysis: To 10 mL of the portion of *Sample solution* retained from the test for *Color of Solution* add a drop of phenolphthalein TS.
  Acceptance criteria: The solution is colorless: NMT 0.25 mL of 0.01 N sodium hydroxide is required to change the color of the indicator to pink.
- **WATER DETERMINATION,** *Method Ia* ⟨**921**⟩**:** 3.0%–5.0%

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers. Store at room temperature.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Sodium Picosulfate RS
  USP Sodium Picosulfate Related Compound A RS