

Status: Currently Official on 14-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-297C0CDF-07F1-4B4F-93B5-EABA7220A086_4_en-US
DOI: https://doi.org/10.31003/USPNF_M11200_04_01
DOI Ref: t5bla

© 2025 USPC
Do not distribute

Caffeine and Sodium Benzoate Injection

DEFINITION

Caffeine and Sodium Benzoate Injection is a sterile solution containing equal amounts of Caffeine and Sodium Benzoate in Water for Injection. It contains NLT 90.0% and NMT 110.0% of the labeled amounts of anhydrous caffeine ($C_8H_{10}N_4O_2$) and sodium benzoate ($C_7H_5NaO_2$).

IDENTIFICATION

Change to read:

- **A.** [▲ SPECTROSCOPIC IDENTIFICATION TESTS \(197\), Infrared Spectroscopy: 197M](#) ▲ (CN 1-MAY-2020)

Sample: Use the residue from the Assay for *Caffeine*.

Acceptance criteria: Meets the requirements

- **B.**

Analysis: Dip the end of a platinum wire into a portion of Injection, and introduce it into a nonluminous flame.

Acceptance criteria: The flame is colored intensely yellow.

- **C.**

Analysis

Part 1: Add a few drops of ferric chloride TS to a 0.5-mL portion of Injection.

Part 2: Add 3 N hydrochloric acid to another portion of Injection.

Acceptance criteria: The criteria in *Part 1* and *Part 2* must both be met.

Part 1: A salmon-colored precipitate is formed.

Part 2: A white precipitate is formed.

ASSAY

- **CAFFEINE**

Sample solution: A volume of Injection equivalent to 250 mg each of caffeine and sodium benzoate

Analysis: Transfer the *Sample solution* with the aid of 5 mL of water to a small separator, add 1 drop of phenolphthalein TS, and add 0.1 N sodium hydroxide, dropwise, until a permanent pink color is just produced. Shake the mixture with three or more 20-mL portions of chloroform to effect complete extraction of the caffeine, passing each chloroform extract through a small filter previously moistened with chloroform into a tared dish. Retain the water layer for the Assay for *Sodium Benzoate*. Wash the stem of the separator, the filter, and the funnel with 10 mL of hot chloroform, adding the washings to the dish. Evaporate the combined chloroform solutions on a steam bath, adding 2 mL of alcohol just before the last trace of chloroform is expelled. Complete the evaporation of the solvent, dry the residue, consisting of caffeine ($C_8H_{10}N_4O_2$), at 80° for 4 h. Cool, and weigh.

Acceptance criteria: 90.0%–110.0%

- **SODIUM BENZOATE**

Sample solution: Use the water layer obtained in the Assay for *Caffeine*.

Titrimetric system

Mode: Direct titration

Titrant: 0.1 N hydrochloric acid VS

Endpoint detection: Visual

Analysis: Add 75 mL of ether and 5 drops of methyl orange TS to the *Sample solution*. Titrate with *Titrant*, and shake vigorously until a permanent pink color is produced in the water layer. Each mL of 0.1 N hydrochloric acid is equivalent to 14.41 mg of sodium benzoate ($C_7H_5NaO_2$).

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

- **BACTERIAL ENDOTOXINS TEST (85):** NMT 0.7 USP Endotoxin Unit/mg of caffeine and sodium benzoate, based on the total, in mg, of the labeled amounts
- **pH (791):** 6.5–8.5
- **OTHER REQUIREMENTS:** It meets the requirements in [Injections and Implanted Drug Products \(1\)](#).

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in single-dose containers, preferably of Type I glass.

- [USP REFERENCE STANDARDS \(11\)](#)
[USP Caffeine RS](#)

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

Topic/Question	Contact	Expert Committee
CAFFEINE AND SODIUM BENZOATE INJECTION	Documentary Standards Support	SM42020 Small Molecules 4

Chromatographic Database Information: [Chromatographic Database](#)

Most Recently Appeared In:

Pharmacopeial Forum: Volume No. Information currently unavailable

Current DocID: GUID-297C0CDF-07F1-4B4F-93B5-EABA7220A086_4_en-US

DOI: https://doi.org/10.31003/USPNF_M11200_04_01

DOI ref: [t5bla](#)

OFFICIAL