Sulfamethoxazole

C_{10}H_{11}N_{3}O_{5}S 253.28
Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)-;
N^1-(5-Methyl-3-isoxazolyl)sulfanilamide [723-46-6]; UNII: JE42381TNV.

DEFINITION
Sulfamethoxazole contains NLT 98.0% and NMT 102.0% of sulfamethoxazole (C_{10}H_{11}N_{3}O_{5}S), calculated on the dried basis.

IDENTIFICATION
Change to read:

• A. **Spectroscopic Identification Tests** (197), *Infrared Spectroscopy*: 197K \( \text{or} \ 197A \) \( \text{IRA} \ 1\text{-May-2021} \)

• B. The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY
Change to read:

• Procedure

  **Buffer**: 13.6 g/L of potassium dihydrogen phosphate adjusted with a 20-g/L solution of potassium hydroxide to a pH of 5.3

  **Mobile phase**: Methanol and Buffer (30:70)

  **Standard solution**: 0.1 mg/mL \( \text{IRA} \ 1\text{-May-2021} \) of USP Sulfamethoxazole RS \( \text{IRA} \ 1\text{-May-2021} \) in Mobile phase. Sonicate at 45° with intermittent shaking to dissolve before final dilution.

  **System suitability solution**: 0.1 mg/mL each of USP Sulfamethoxazole RS and USP Sulfamethoxazole Related Compound A RS in Mobile phase. Sonicate at 45° with intermittent shaking to dissolve before final dilution. \( \text{IRA} \ 1\text{-May-2021} \)

  **Sample solution**: 0.1 mg/mL of Sulfamethoxazole in Mobile phase. Sonicate at 45° with intermittent shaking to dissolve before final dilution.

  **Chromatographic system**
  (See *Chromatography (621), System Suitability*,)

    **Mode**: LC

    **Detector**: UV 210 nm

    **Column**: 4-mm × 25-cm; 5-µm packing L7

    **Flow rate**: 0.9 mL/min

    **Injection volume**: 20 µL
System suitability

Samples: Standard solution and (IRA 1-May-2021) Standard solution

[Note—The relative retention times for sulfamethoxazole and sulfamethoxazole related compound A are 1.0 and 1.2, respectively.]

Suitability requirements

Resolution: NLT 3.5 between sulfamethoxazole and sulfamethoxazole related compound A, System suitability solution, (IRA 1-May-2021)

Relative standard deviation: NMT 0.73%, Standard solution, (IRA 1-May-2021)

Analysis

Samples: Standard solution and Sample solution

Calculate the percentage of sulfamethoxazole (C_{10}H_{11}N_{3}O_{3}S) in the portion of Sulfamethoxazole taken:

\[
\text{Result} = \frac{r_U}{r_s} \times \frac{C_S}{C_U} \times 100
\]

\(r_U\) = peak response of sulfamethoxazole from the Sample solution
\(r_s\) = peak response of sulfamethoxazole from the Standard solution
\(C_S\) = concentration of USP Sulfamethoxazole RS in the Standard solution (mg/mL)
\(C_U\) = concentration of Sulfamethoxazole in the Sample solution (mg/mL)

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

• Residue on Ignition (281): NMT 0.1%

Change to read:

• Organic Impurities

Buffer, Mobile phase, System suitability solution, (IRA 1-May-2021) and Chromatographic system: Proceed as directed in the Assay.

^ (IRA 1-May-2021)

Peak identification solution: 1 µg/mL each of USP Sulfamethoxazole Related Compound A RS, USP Sulfamethoxazole Related Compound B RS, USP Sulfamethoxazole Related Compound C RS, USP Sulfanilic Acid RS, and USP Sulfanilamide RS in Mobile phase. Sonicate, if necessary, to dissolve before final dilution.

^Sensitivity solution: 0.3 µg/mL of USP Sulfamethoxazole RS in Mobile phase. Sonicate, if necessary, to dissolve before final dilution. (IRA 1-May-2021)

Standard solution: 1 µg/mL each of USP Sulfamethoxazole RS and USP Sulfamethoxazole Related Compound F RS in Mobile phase. Sonicate, if necessary, to dissolve before final dilution.

Sample solution: 1 mg/mL of Sulfamethoxazole in Mobile phase. Sonicate at 45° with intermittent shaking to dissolve before final dilution.

System suitability

Samples: System suitability solution, Sensitivity solution, (IRA 1-May-2021) and Standard solution

Suitability requirements

Resolution: NLT 3.5 between sulfamethoxazole and sulfamethoxazole related compound A, System suitability solution, (IRA 1-May-2021)
**Relative standard deviation:** NMT 5.0% \( \uparrow \) each \( \uparrow \) (IRA 1-May-2021) for sulfamethoxazole \( \uparrow \) and sulfamethoxazole related compound F \( \uparrow \) (IRA 1-May-2021) *Standard solution*

\( \uparrow \) **Signal-to-noise ratio:** NLT 10, *Sensitivity solution* \( \uparrow \) (IRA 1-May-2021)

### Analysis

**Samples:** *Peak identification solution, Standard solution, and Sample solution*

Calculate the percentage of sulfamethoxazole related compound F in the portion of Sulfamethoxazole taken:

\[
\text{Result} = \left( \frac{r_S}{r_U} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

- \( r_U \) = peak response of sulfamethoxazole related compound F from the *Sample solution*
- \( r_S \) = peak response of sulfamethoxazole related compound F from the *Standard solution*
- \( C_S \) = concentration of USP Sulfamethoxazole Related Compound F RS in the *Standard solution* (mg/mL)
- \( C_U \) = concentration of Sulfamethoxazole in the *Sample solution* (mg/mL)

Calculate the percentage of any \( \uparrow \) other \( \uparrow \) (IRA 1-May-2021) individual impurity in the portion of Sulfamethoxazole taken:

\[
\text{Result} = \left( \frac{r_I}{r_S} \right) \times \left( \frac{C_S}{C_U} \right) \times 100
\]

- \( r_I \) = peak response of any \( \uparrow \) other \( \uparrow \) (IRA 1-May-2021) individual impurity from the *Sample solution*
- \( r_S \) = peak response of sulfamethoxazole from the *Standard solution*
- \( C_S \) = concentration of USP Sulfamethoxazole RS in the *Standard solution* (mg/mL)
- \( C_U \) = concentration of Sulfamethoxazole in the *Sample solution* (mg/mL)

**Acceptance criteria:** See *Table 1*. The reporting threshold is 0.03%.

### Table 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative Retention Time</th>
<th>Acceptance Criteria, NMT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfanilic acid</td>
<td>0.26</td>
<td>0.10</td>
</tr>
<tr>
<td>Sulfanilamide</td>
<td>0.35</td>
<td>0.10</td>
</tr>
<tr>
<td>Sulfamethoxazole related compound F</td>
<td>0.45</td>
<td>0.10</td>
</tr>
<tr>
<td>Sulfamethoxazole related compound C</td>
<td>0.50</td>
<td>0.10</td>
</tr>
<tr>
<td>Sulfamethoxazole</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>Sulfamethoxazole related compound A</td>
<td>1.2</td>
<td>0.10</td>
</tr>
<tr>
<td>Sulfamethoxazole related compound B</td>
<td>2.1</td>
<td>0.10</td>
</tr>
<tr>
<td>Name</td>
<td>Relative Retention Time</td>
<td>Acceptance Criteria, NMT (%)</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>-------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Any individual unspecified impurity</td>
<td>—</td>
<td>0.10</td>
</tr>
<tr>
<td>Total impurities</td>
<td>—</td>
<td>0.30</td>
</tr>
</tbody>
</table>

**SPECIFIC TESTS**

- **Loss on Drying** *(731)*
  
  **Analysis:** Dry at 105° for 4 h.
  
  **Acceptance criteria:** NMT 0.5%

**ADDITIONAL REQUIREMENTS**

- **Packaging and Storage:** Preserve in well-closed, light-resistant containers. Store at room temperature.
  
  **Change to read:**

- **USP Reference Standards** *(11).*
  
  **USP Sulfamethoxazole RS**
  
  **USP Sulfamethoxazole Related Compound A RS**
  
  $N$-{(4-[$N$-(5-Methylisoxazol-3-yl)sulfamoyl]phenyl)acetamide.
  
  \[C_{12}H_{13}N_3O_4S\] 295.31
  
  **USP Sulfamethoxazole Related Compound B RS**
  
  4-Amino-$N$-{(4-[$N$-(5-methylisoxazol-3-yl)sulfamoyl]phenyl)benzenesulfonamide.
  
  \[C_{16}H_{16}N_4O_5S_2\] 408.45
  
  **USP Sulfamethoxazole Related Compound C RS**
  
  5-Methylisoxazol-3-amine.
  
  \[C_4H_6N_2O\] ▲98.11 (IRA 1-May-2021)
  
  **USP Sulfamethoxazole Related Compound F RS**
  
  4-Amino-$N$-(3-methylisoxazol-5-yl)benzenesulfonamide.
  
  \[C_{10}H_{11}N_3O_3S\] 253.28
  
  **USP Sulfanilamide RS**
  
  4-Aminobenzenesulfonamide.
  
  \[C_6H_8N_2O_2S\] 172.20
  
  **USP Sulfanilic Acid RS**
  
  4-Aminobenzenesulfonic acid.
  
  \[C_6H_7NO_3S\] 173.19