COMPONENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole)
$C_{10}H_{11}N_3O_3S$; [723-46-6]
(2) Water
(3) Aqueous HCl; (4) Aqueous NaOH
(5) Aqueous ethanol
(6) Methanol

EVALUATOR:
Anthony N. Paruta
Department of Pharmaceutics
University of Rhode Island
Kingston, Rhode Island, USA
and
Ryszard Piekos
Faculty of Pharmacy, University of Gdansk
Gdansk, Poland 1986

CRITICAL EVALUATION:

The aqueous solubility data on the above compound are summarized in Table I. Yamazaki's (2) value was the only value available at 303K, and is not considered further. It is lower than those at 298K (4,6), thus probably unreasonable. Rudy and Senkowski (4) and Shah et al. (6) give identical values for the aqueous solubility at 289K. The solubility values can thus be given as 2 x 10^{-3} mol dm^{-3} in water at 298K. Kitao et. al. (3) determined the solubility at 310K at a pH value of 4. Since there are no concurring values (1,5) no recommended value can be given for this temperature. The value of Kitao et al. (3) is somewhat similar to that of Ghanem et al. (5), which is interesting since it would be expected that a broad invarient solubility isotherm over a span of pH values should exist. Thus, even though these values are similar, the solubility suggested by Ghanem et al. (5) is probably valid, and can be proposed as the tentative value.

Table I: Solubility of Sulfamethoxazole in water at various temperatures

	10^3 mol dm^{-3} (*indicates mol kg^{-1})		
Reference	298K	303K	310K
1	-	-	4.11
2	-	1.59	-
3	-	-	2.48 (pH=4)
4	2.0	-	-
5	-	-	2.37
6	2	-	-

For ampholytes of this type, solubility can be enhanced by the addition of either acids or bases. The condition produce a more water soluble cationic species (protonation) under acidic conditions, and the more water soluble anionic form under basic conditions at high pH. In two reports (7,8), the solubility was determined in 0.1N HCl both at 298K and 310K. Ogata et al. (7) records a value of 1.24 x 10^{-2} mol dm^{-3} in 0.1N HCl at 310K which is 6.2 times the solubility in water. Shah et al. (8) give a value of 1 x 10^{-4} mol dm^{-3} at a pH = 1, which is clearly incorrect being only a small fraction of the solubility in water (about 5%). However, at a concentration of 0.84N HCl (pH = 0.076) at 298K, a value of 1.12 x 10^{-2} mol dm^{-3} is reported which is in line with the value of Ogata et al. (7) being about 5.6 times the solubility in water. The value of Shah et al. (8) in 0.84N HCl is some 95 times greater than that in 0.1N HCl. In this context it might be instructive to point out the trend (magnitude enhancement) by comparing the solubility of sulfamethoxazole in different systems. The recommended values at 298K are 2 x 10^{-3} mol dm^{-3} in water, 63 x 10^{-3} mol dm^{-3} in 0.1N NaOH, 149 x 10^{-3} mol dm^{-3} in 95% ethanol in water and 350 x 10^{-3} mol dm^{-3} in methanol. There is a 31 fold increase in solubility in 0.1N NaOH no doubt due to the formation of the anionic form of the compound which has a much higher aqueous solubility. There is a dramatic shift in pH from near neutrality to pH = 13, a strong alkaline solution that forms a water soluble sodium salt of this compound. In methanol, there is a 175 fold increase in solubility due to the semipolar nature of solute and solvent. In 95% ethanol in water (10-12) there is about a 75 fold increase in solubility. The enhancements are quite striking and illustrate the significant latitude that can be used. The solubility of this compound was given by Rudy and Senkowski (9) and Shah et al. (8) in 1973 and 1981 respectively are in excellent agreement and a recommended value of 6.3 x 10^{-2} mol dm^{-3} can be given in aqueous 0.1N NaOH solution at 298K.

Further, the values of solubility in methanol were given by these workers (8,9) and were also in excellent agreement and is given as 0.35 mol dm^{-3} at 298K. The recommended value in 95% ethanol in water is 0.13 mol dm^{-3} at 298K.

REFERENCES:

(1) Anderson, G.W.; Faith, H.E.; Marson, H.W.; Winnek, P.S.; Roblin, R.O., Jr. *J. Am. Chem. Soc.* 1942, *64*, 2902-5.
(2) Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N.; *Yakuzaigaku* 1967, *27(1)*, 37-40.
(3) Kitao, K,; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. *Chem. Pharm. Bull.* 1973, *21*, 2417-26.
(4) Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, *2*, 467-86.
(5) Ghanem, A.; Meshali, M.; Ibraheem, Y. *J. Pharm. Pharmacol.* 1980, *32*, 675-7.
(6) Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)*, 611-13.

REFERENCES: Continuation

(7) Rudy, B.C.; Senkowski, B.Z.; *Anal. Profiles Drug Subst.* 1973, 2, 467-86.
(8) Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)*, 611-13.
(9) Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subts.* 1973, 2, 467-86.
(10) Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)*, 611-13.
(11) Rudy, B.C.; Senkowski, B.Z., *Anal. Profiles Drug Subst.* 1973, 2, 467-86.
(12) Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)*, 611-13.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Water; H_2O; [7732-18-5]	Anderson, G.W.; Faith, H.E.; Marson, H.W.; Winnek, P.S.; Roblin, R.O.,Jr. *J. Am. Chem. Soc.* 1942, *64*, 2902-5.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in water at 37°C is 104 mg/100 cm^3 solution (4.11 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Excess sulfonamide in water was heated and stirred on a steam bath for 30 min. The suspension was then agitated for 24 h in a thermostat. A sample of the satd soln was withdrawn through a glass filter, dild, and analyzed by the Marshall method (1) using a General Electric recording spectrophotometer for comparing the colors developed with those of the standards.

SOURCE AND PURITY OF MATERIALS:

The sulfonamide, mp 169-70°C (cor) was prepd by the authors. Anal: %C 47.4 (calcd 47.4); %H 4.2 (4.4); %N 16.5 (16.6).

Purity of the water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

1. Bratton, A.C.; Marshall, E.K., Jr. *J. Pharmacol.* 1939, *66*, 4.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfisomezole)*; $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Water; H_2O; [7732-18-5]	Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1)*, 37-40.
VARIABLES: One temperature: 30°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfisomezole* in water at 30°C is 1.59 mmol/L (0.403 g dm^{-3}, compiler).

*Another common trivial name is sulfamethoxazole.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

Sulfisomezole* (0.5 g) was placed in an L-shaped tube together with 20 ml of water. The mixt was shaken in a thermostat until equilibrium was attained. The sulfisomezole* was assayed in the supernatant spectrophotometrically at 545 nm on a Beckman DU spectrophotometer. The results were taken from a calibration graph.

SOURCE AND PURITY OF MATERIALS:

Nothing specified

ESTIMATED ERROR:

Soly: not specified

Temp: ±1°C (authors)

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Water; H_2O; [7732-18-5]	Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. *Chem. Pharm. Bull.* 1973, *21*, 2417-26.
VARIABLES:	**PREPARED BY:**
One temperature: 37°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in water at 37°C is 2.48 mmol dm^{-3} solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Soly was detd by continuously adjusting the pH of the aq soln to 4 with 0.05N NaOH. The concn. of sulfamethoxazole was detd by diazotization.	Comm available sulfamethoxazole (source not specified) was used as supplied. Deionized water was used.
	ESTIMATED ERROR: Soly: not specified Temp: ±1°C (authors).
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Water; H_2O; [7732-18-5]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, *2*, 467-86.
VARIABLES: One temperature" 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in water at 25°C is 0.5 mg/ml (2.0×10^{-3} mol dm^{-3}, compiler). [a]

[a]The temperature and all auxilliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with the solvent overnight at const temp. (25°C) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken and its concn was detd by uv spectrophotometry after suitable diln.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. The distd and deionized water of high resistivity was used.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)

Temp: not specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Water; H_2O; [7732-18-5]	Ghanem, A.; Meshali, M.; Ibraheem, Y. *J. Pharm. Pharmacol.* 1980, *32*, 675-7.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in water at 37°C is 0.6 g litre^{-1} (2 x 10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethoxazole was added to 15 ml of water in a 30-ml glass stoppered bottle which was rotated on a water bath at 37°C until equilibrium was attained. The sample was filtered and the sulfonamide was assayed spectrophotometrically at 265 nm after dilg with 0.1M HCl. A coulometric assay gave similar results.

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole was from Kahira Pharm and Chem Ind Co. Egypt.

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: detns were carried out at least in duplicate (authors).

Temp: ± 1°C (authors).

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Water; H_2O; [7732-18-5]	Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)*, 611-13.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in water at 25°C is 0.5 mg/ml (2×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
The solubility of sulfamethoxazole was determined by the method specified in USP XX (1).	Sulfamethoxazole was a research compd purchased from Hoffman - LaRoche, Nutley, N.J. Its purity was not specified. The purity of water was not specified.
	ESTIMATED ERROR: Nothing specified
	REFERENCES: 1. *"The United States Pharmacopeia"*, 20th rev., U.S. Pharmacopeial Convention, Rockville, Md., 1980, p. 120

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Hydrochloric acid; HCl; [7647-01-0] (3) Water; H_2O; [7732-18-5]	Ogata, H.; Shibazaki, T.; Inoue, T.; Ejima, A. *Chem. Pharm. Bull.* 1979 *27(6)*, 1281-6.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in 0.1N HCl at 37°C is 3.140 mg/ml (1.240×10^{-2} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
A centrifuge tube contg 30 ml of 0.1N HCl and 0.5-3.0 g of the sulfamethoxazole powder was tightly sealed and shaken at 37°C. The concn of the dissolved drug was detd spectrophotometrically following filtration through a Millipore filter (type EH, pore size 0.5 μm), and the procedure was repeated every 24 h until a const concn was obtained.	Comm available 500-mg uncoated tablets of sulfamethoxazole were used. Hydrochloric acid was of reagent grade.
	ESTIMATED ERROR: Nothing specified
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Hydrochloric acid; HCl;[7647-01-0] (3) Water; H_2O; [7732-18-5]	Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)*, 611-13.
VARIABLES: Concentration of HCl	**PREPARED BY:** R.Piekos

EXPERIMENTAL VALUES:

Concentration of HCl, N	Solubility at 25°C	
	mg/ml	mol dm^{-3} [a]
0.1	0.03	1×10^{-4}
0.84	2.85	1.12×10^{-2}

[a]Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The solubility of sulfamethoxazole was determined by the method specified in USP XX (1).

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole was a research compd purchased from Hoffman - LaRoche, Nutley, N.J. Its purity was not specified.

The source and purity of hydrochloric acid was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

1. *"The United States Pharmacopeia"*, 20th rev., U.S. Pharmacopeial Convention, Rockville, Md., 1980, p. 120.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Sodium hydroxide; NaOH; [1310-73-2] (3) Water; H_2O; [7732-18-5]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, *2*, 467-86.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in a 0.1N NaOH solution at 25°C is 16.0 mg/ml (6.32×10^{-2} mol dm^{-3}, compiler).[a]

[a]The temperature and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with the solvent overnight at const temp (25°) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant solution was then taken and its concn was detd by uv spectrophotometry after suitable diln.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. Reagent grade NaOH was used. The distd and deionized water of high resistivity was used.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)
Temp: not specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Sodium hydroxide; NaOH; [1310-73-2] (3) Water; H_2O; [7732-18-5]	Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)* 611-13.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in a 0.1N NaOH solution at 25°C is 16 mg/ml (6.3×10^{-2} dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The solubility of sulfamethoxazole was determined by the method specified in USP XX (1).

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole was a research compd purchased from Hoffman - LaRoche, Nutley, N.J. Its purity was not specified.

The source and purity of NaOH and water was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

1) *"The United States Pharmacopeia"*, 20th rev., U.S. Pharmacopeial Convention, Rockville, Md., 1980 p. 120.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Sodium chloride; NaCl; [7647-14-5] (3) Water; H_2O; [7732-18-5]	Hirano, K.; Ichibashi, T.; Yamada, H. *Chem. Pharm. Bull.* 1981, *29(3)*, 817-27.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in a 0.9% NaCl solution at 37°C is 0.61 mg/ml (2.4×10^{-3} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess amt of powdered sulfamethoxazole was shaken well at 37°C with a 0.9% NaCl soln until attaining satn. The undissolved crystals were removed by filtration through a G5 glass filter or by centrifugation, and the concn of solute in the filtrate or supernatant was assayed spectrophotometrically at 267 nm, after diln with EtOH - H_2O (1:1, v/v), using a Perkin Elmer UV-VIS spectrophotometer (Hitachi Co., Ltd., Tokyo)

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole was synthesized by the authors and was of medicinal grade. The remaining materials were of anal or reagent grade.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Phosphoric acid, disodium salt Na_2HPO_4; [7558-94-4] (3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0] (4) Water; H_2O; [7732-18-5]	Riess, W. *Intern. Congr. Chemotherapy, Proc., 3rd, Stuttgart* 1963, *1*, 627-32.
	PREPARED BY: R. Piekos

VARIABLES:

One temperature: 20°C; one pH: 7.4

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in a M/15 Sörensen buffer solution (pH 7.4) at 20°C is 930 mg% (3.67×10^{-2} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Sörensen buffer solns of pH varying between 7 and 8 were prepd, satd with sulfamethoxazole at 20°C, their pH was measured at equilibrium, and the sulfamethoxazole was assayed colorimetrically. The measured pH values were then plotted against concn, and the soly at pH 7.4 was detd by interpolation (personal communication).	Nothing specified
	ESTIMATED ERROR: Nothing specified
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfisomezole)*; $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4] (3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0] (4) Water; H_2O; [7732-18-5]	Yamazaki, M; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku* 1967, *27(1)*, 37-40.
	PREPARED BY: R. Piekos

VARIABLES:

One temperature: 30°C; one pH: 7.4

EXPERIMENTAL VALUES:

Solubility of sulfisomezole* in a phosphate buffer solution of pH 7.4[a] (μ = 0.17) at 30°C is 20.7 mmol/L (5.24 g dm^{-3}, compiler).

[a]At the end of experiment the pH was 6.9

*Another common trivial name is sulfamethoxazole.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Sulfisomezole* (0.5 g) was placed in an L-shaped tube together with 20 ml of the buffer soln. The mixt was shaken in a thermostat until equilibrium was attained. The sulfisomezole* was assayed in the supernatant spectrophotometrically at 545 nm on a Beckmann DU spectrophotometer. The results were taken from a calibration graph.	Nothing specified
	ESTIMATED ERROR: Soly and pH: not specified Temp: ±1°C (authors)
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4] (3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0] (4) Water; H_2O; [7732-18-5]	Hekster, Y.A.; Vree, T.B.; Damsma, J.E.; Friesen, W.T. *J. Antimicrob. Chemother.* 1981, 8, 133-44.
VARIABLES: pH	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

pH	Solubility at 25°C	
	mg/l	10^3 mol dm^{-3} [a]
5.5	300	1.18
7.5	1900	7.50

[a]Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Satd solns of sulfamethoxazole were prepd in phosphate buffers of pH 5.5 and 7.5 at room temp (25°C). The concn of the solute was measured by means of a Spectra Physics 3500B high-performance liquid chromatograph equipped with a column oven (Model 748) and a Pye-Unicam LC-UV spectrophotometric detector. The detector was connected to a 1-mV recorder. A stainless steel column (10 cm x 4.6 mm i.d.) was packed with Lichrosorb RPS, 5 µm, obtained from Chrompack. An injection loop of 100 µl was used. The oven temp was 40°C. Detection of sulfamethoxazole was performed at 260 nm.	The source and purity of the materials was not specified.
	ESTIMATED ERROR: The detection limit of the solute by HPLC was 0.5 mg/l (authors). The error in temperature and pH was not specified.
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4] (3) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0] (4) Water; H_2O; [7732-18-5]	Meshali, M.; El Sabbagh, H.; Ghanem, A.; Foda, A. *Pharmazie* 1983, *38(6)*, 403-6.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Equilibrium solubility of sulfamethoxazole in a phosphate buffer solution of pH 7.2, at 37°C, is 0.6% (2×10^{-2} mol kg^{-1} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
A tablet of sulfamethoxazole was placed in 500 ml of a phosphate buffer of pH 7.2 and stirred at 37°C. Samples were taken at time intervals and the solute concn was detd by the method reported by the authors (1).	Sulfamethoxazole tablets were picked up from the market. They satisfied the USP requirements for uniformity of wt and the BP requirements for uniformity of content. The source and purity of the remaining materials were not specified.
	ESTIMATED ERROR: Nothing specified.
	REFERENCES: 1. Ghanem, A.; Meshali, M.; Foda, A. *J. Pharm. Pharmacol* 1979, *31*, 122.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Aminoacetic acid (glycine); $C_2H_5NO_2$; [56-40-6] (3) Hydrochloric acid; HCl; [7647-01-0] (4) Sodium chloride; NaCl; [7647-14-5] (5) Water; H_2O; [7732-18-5]	Meshali, M.; El Sabbagh, H.; Ghanem, A.; Foda, A. *Pharmazie*, 1983, *38(6)*, 403-6.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Equilibrium solubility of sulfamethoxazole in artificial gastric juice (0.5 g glycine, 0.35 g NaCl and 9.4 ml HCl per liter of solution; pH 1.1) at 37°C is 0.338% (1.33×10^{-2} mol kg^{-1} solution - compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
A tablet of sulfamethoxazole was placed in 500 ml of artificial gastric juice of pH 1.1, and the suspension was stirred at 37°C. Samples were taken at time intervals and the solute concn was detd by the method reported by the authors.	Sulfamethoxazole tablets were picked up from the market. They satisfied the USP requirements for uniformity of wt and the BP requirements for uniformity of content. The source and purity of the remaining materials were not specified.
	ESTIMATED ERROR: Nothing specified.
	REFERENCES: 1. Ghanem. A.; Meshali, M.; Foda, A. *J. Pharm. Pharmacol.* 1979, *31*, 122.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4] (3) Phosphoric acid, monopotassium salt KH_2PO_4; [7778-77-0] (4) Sodium chloride; NaCl; [7647-14-5] (5) Water; H_2O; [7732-18-5]	Hirano, K.; Ichihashi, T.; Yamada, H.; *Chem. Pharm. Bull.* 1981, *29(3)*, 817-27.
VARIABLES: One temperature: 37°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in a 1/15M phosphate buffer solution of pH 7.25, isotonized with NaCl, at 37°C, is 5.7 mg/ml (2.2×10^{-2} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
An excess amt of powdered sulfamethoxazole was shaken well at 37°C with 1/15M phosphate buffer of pH 7.25, isotonized with NaCl, until attaining satn. The undissolved crystals were removed by filtration through a G5 glass filter or by centrifugation, and the concn of solute in the filtrate or supernatant was assayed spectrophotometrically at 267 nm. after diln with EtOH - H_2O (1:1, v/v), using a Perkin Elmer UV-VIS spectrophotometer (Hitachi Co., Ltd., Tokyo).	Sulfamethoxazole was synthesized by the authors and was of medicinal grade. The remaining materials were of anal or reagent grade.
	ESTIMATED ERROR: Nothing specified
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Ethanol; C_2H_6O; [64-17-5] (3) Water; H_2O; [7732-18-6]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, 2, 467-86
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in 95% ethanol at 25°C is 37.8 mg/ml (0.149 mol dm^{-3}, compiler).[a]

[a]The temperature and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with the solvent overnight at const temp (25°C) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken, weighed and the solvent removed in a vacuum oven. The wt of solute was detd after the residue had been dried to const wt. All weighing was done on a Mettler microbalance using microanal techniques.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. The solvent was purchased Reagent Grade and used without further purification.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)
Temp: not specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Ethanol; C_2H_6O; [64-17-5] (3) Water; H_2O; [7732-18-5]	Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)*, 611-13.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in 95% ethanol at 25°C is 30 mg/ml (0.12 mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
The solubility of sulfamethoxazole was determined by the method specified in USP XX (1).	Sulfamethoxazole was a research compd purchased from Hoffman - LaRoche, Nutley, N.J. Its purity was not specified. The source and purity of the 95% EtOH was not specified.
	ESTIMATED ERROR: Nothing specified
	REFERENCES: 1. *"The United States Pharmacopeia"*, 20th rev., U.S. Pharmacopeial Convention, Rockville, Md., 1980, p. 120.

COMPONENTS:

(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6]

(2) Bovine serum albumin

(3) Phosphoric acid, disodium salt; Na_2HPO_4; [7558-94-4]

(4) Phosphoric acid, monopotassium salt; KH_2PO_4; [7778-77-0]

(5) Sodium chloride; NaCl; [7647-14-5]

(6) Water; H_2O; [7732-18-5]

VARIABLES:

One temperature: 37°C; one pH: 7.25

ORIGINAL MEASUREMENTS:

Hirano, K.; Yamada, H.

J. Pharm. Sci. 1982, *71(5)*, 500-5.

PREPARED BY:

R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in a 2% (w/v) bovine serum albumin in pH 7.25 phosphate buffer (0.067 M Na_2HPO_4-KH_2PO_4) isotonized with NaCl, at 37°C, is 7.2 mg/ml (2.8×10^{-2} mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The previously developed method was employed (1). An excess of powd sulfamethoxazole was shaken well at 37°C with the 2% bovine serum albumin in pH 7.25 phosphate buffer isotonized with NaCl until attaining satn. The undissolved crystals were removed by filration through a G5 glass filter or by centrifugation, and the concn of solute in the filtrate or supernatant was assayed spectrophotometrically at 267 nm using a Perkin Elmer UV-VIS spectrophotometer (Hitachi Co., Ltd., Tokyo).

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole was synthesized by the authors and was of medicinal grade. Bovine serum albumin (purity not specified) was from Sigma Chemical Co., St. Louis, Mo. The remaining materials were of anal or reagent grade.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

1. Hirano, K.; Ichihashi, T.; Yamada, H. *Chem. Pharm. Bull.* 1981, *29(3)*, 817.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) 1,4,7,10,13,16-Hexaoxacyclooctadecane (18-C-6); $C_{12}H_{24}O_6$; [17455-13-9] (3) Hydrochloric acid; HCl; [7647-01-0] (4) Water; H_2O; [7732-18-5]	Takayama, K; Nambu, N.; Nagai, T. *Chem. Pharm. Bull.* 1978, *26(10)*, 2965-70.
	PREPARED BY: R. Piekos

VARIABLES:

Temperature

EXPERIMENTAL VALUES:

t/°C	Saturated concentration of sulfamethoxazole after decomplexation of its 1:1 complex with 18-C-6 in 0.2N HCl 10^2M
30	1.11
35	1.31
40	1.64

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of the complex was dissolved in 50 ml of 0.2N HCl. The sampling was done by a 1-ml pipet fitted with a G-4 glass filter. The concentration of the sulfonamide was detd by uv spectrophotometry after dilg with 0.2N HCl.

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole (Shionogi Pharmaceutical Co.) was recrystd from a 30% (V/V) Me_2CO-H_2O soln. 18-C-6 was of the reagent grade. The 1:1 complex was prepd by the authors. Purity of the HCl soln was not specified.

ESTIMATED ERROR:

Nothing specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide,4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) D-Glucitol (sorbitol); $C_6H_{14}O_6$; [50-70-4] (3) Water; H_2O; [7732-18-5]	Ghanem, A.; Meshali, M.; Ibraheem, Y. *J. Pharm. Pharmacol.* 1980, *32*, 675-7.
VARIABLES: Concentration of sorbitol	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Concentration of sorbitol Weight%	Solubility at 37°C	
	g litre^{-1}	10^3 mol dm^{-3} [a]
0.5	0.60	2.37
1.0	0.595	2.35
1.5	0.60	2.37

[a]Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
An excess of sulfamethoxazole was added to 15 ml of sorbitol soln in 30-ml glass-stoppered bottles which were rotated on a water bath at 37°C until equilibrium was attained. Samples were filtered and the sulfonamide was assayed spectrophotometrically at 265 nm after dilg with 0.1M HCl. Coulometric assays gave similar results.	Sulfamethoxazole was from Kāhira Pharm and Chem Ind Co, Egypt. Sorbitol was purchased from El-Nasr Chem Co, Egypt. Distd waster was used.
	ESTIMATED ERROR: Soly: detns were carried out in duplicate (authors) Temp: ±1°C (authors)
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Mannitol; $C_6H_{14}O_6$; [87-78-5] (3) Water; H_2O; [7732-18-5]	Ghanem, A.; Meshali, M.; Ibraheem, Y. *J. Pharm. Pharmacol.* 1980, *32*, 675-7.
VARIABLES: Concentration of mannitol	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Concentration of mannitol Weight%	Solubility at 37°C	
	g litre^{-1}	10^3mol dm^{-3} [a]
0.5	0.615	2.43
1.0	0.605	2.39
1.5	0.603	2.38

[a]Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethoxazole was added to 15 ml of mannitol soln in 30-ml glass-stoppered bottles which were rotated on a water bath at 37°C until equilibrium was attained. Samples were filtered and the sulfonamide was assayed spectrophotometrically at 265 nm after dilg with 0.1M HCl. Coulometric assays gave similar results.

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole was from Kahira Pharm and Chem Ind Co, Egypt. Mannitol was purchased from El-Nasr Chem Co, Egypt. Distd water was used.

ESTIMATED ERROR:

Soly: detns were carried out in duplicate (authors).
Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Glucose; $C_6H_{12}O_6$; [50-99-7] (3) Water; H_2O; [7732-18-5]	Ghanem, A.; Meshali, M.; Ibraheem, Y. *J. Pharm. Pharmacol.* 1980, *32*, 675-7.
VARIABLES: Concentration of glucose	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Concentration of glucose Weight%	Solubility at 37°C	
	g litre^{-1}	10^3 mol dm^{-3} [a]
0.5	0.67	2.6
1.0	0.755	3.0
1.5	0.76	3.0

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
An excess of sulfamethoxazole was added to 15 ml of glucose soln in 30-ml glass-stoppered bottles which were rotated on a water bath at 37°C until equilibrium was attained. Samples were filtered and the sulfonamide was assayed spectrophotometrically at 265 nm after dilg with 0.1M HCl. Coulometric assays gave similar results.	Sulfamethoxazole was from Kahira Pharm and Chem Ind Co, Egypt. Glucose was purchased from El-Nasr Chem Co, Egypt. Distd water was used.
	ESTIMATED ERROR: Soly: detns were carried out in duplicate (authors). Temp: ±1°C
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Galactose; $C_6H_{12}O_6$; [26566-61-0] (3) Water; H_2O; [7732-18-5]	Ghanem, A.; Meshali, M.; Ibraheem, Y. *J. Pharm. Pharmacol*, 1980, *32*, 675-7.
VARIABLES: Concentration of galactose	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Concentration of galactose Weight%	Solubility at 37°C: g litre^{-1}	Solubility at 37°C: 10^3 mol dm^{-3} [a]
0.5	0.67	2.64
1.0	0.775	3.06
1.5	0.80	3.16

[a] Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:
An excess of sulfamethoxazole was added to 15 ml of galactose soln in 30-ml glass-stoppered bottles which were rotated on a water bath at 37°C until equilibrium was attained. Samples were filtered and the sulfonamide was assayed spectrophotometrically at 265 nm after dilg with 0.1M HCl. Coulometric assays gave similar results.

SOURCE AND PURITY OF MATERIALS:
Sulfamethoxazole was from Kahira Pharm and Chem Ind Co, Egypt. Galactose was purchased from E. Merck.
Distd water was used.

ESTIMATED ERROR:
Soly: detns were carried out in duplicate (authors).
Temp: ±1°C (authors).

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) α-D-Glucopyranoside, β-D-fructofuranosyl- (sucrose); $C_{12}H_{22}O_{11}$; [57-60-1] (3) Water; H_2O; [7732-18-5]	Ghanem, A.; Meshali, M.; Ibraheem, Y. *J. Pharm. Pharmacol.* 1980, *32*, 675-7.
VARIABLES: Concentration of sucrose	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Concentration of sucrose Weight%	Solubility at 37°C	
	g litre^{-1}	10^3 mol dm^{-3} [a]
0.5	0.615	2.43
1.0	0.605	2.39
1.5	0.615	2.43

[a]Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

A excess of sulfamethoxazole was added to 15 ml of sucrose soln in 30-ml glass-stoppered bottles which were rotated on a water bath at 37°C until equilibrium was attained. Samples were filtered and the sulfonamide was assayed spectrophotometrically at 265 nm after dilg with 0.1M HCl. Coulometric assays gave similar results.

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole was from Kahira Pharm and Chem Ind Co, Egypt. Sucrose was purchased.

Purity of the water was not specified.

ESTIMATED ERROR:

Soly: detns were carried out in duplicate (authors).

Temp: ±1°C (authors)

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) D-Glucose, 4-O- α-D-glucopyranosyl- (maltose); $C_{12}H_{22}O_{11}$; [69-79-4] (3) Water; H_2O; [7732-18-5]	Ghanem, A.; Meshali,M.; Ibraheem, Y. *J. Pharm. Pharmacol.* 1980, *32*, 675-7.
VARIABLES: Concentration of maltose	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Concentration of maltose Weight%	Solubility at 37°C	
	g litre^{-1}	10^3 mol dm^{-3} [a]
0.5	0.66	2.6
1.0	0.79	3.1
1.5	0.83	3.3

[a]Calculated by compiler

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of sulfamethoxazole was added to 15 ml of maltose soln in 30-ml glass-stoppered bottles which were rotated on a water bath at 37°C until equilibrium was attained. Samples were filtered and the sulfonamide was assayed spectrophotometrically at 265 nm after dilg with 0.1M HCl. Coulometric assays gave similar results.

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole was from Kahira Pharm and Chem Ind Co, Egypt. Maltose was purchased from Spolek, Czechoslovakia. Distd water was used.

ESTIMATED ERROR:

Soly: detns were carried out in duplicate (authors).

Temp: ±1°C

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Methanol; CH_4O; [67-56-1]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst*, 1973, *2*, 467-86.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in methanol at 25°C is 90.3 mg/ml (0.356 mol dm^{-3}, compiler).[a]

[a]The temperature and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with the solvent overnight at const temp (25°C) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken, weighed and the solvent removed in a vacuum oven. The wt. of solute was detd after the residue had been dried to const wt. All weighing was done on a Mettler microbalance using microanal techniques.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. The solvent was purchased Reagent Grade and used without further purification.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)

Temp: not specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Methanol; CH_4O; [67-56-1]	Shah, N.H.; Lazarus, J.H.; Sheth, P.R.; Jarowski, C.I. *J. Pharm. Sci.* 1981, *70(6)*, 611-13.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in methanol at 25°C is 90 mg/ml (0.35 mol dm^{-3}, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
The solubility of sulfamethoxazole was determined by the method specified in USP XX (1).	Sulfamethoxazole was a research compd purchased from Hoffmann - LaRoche, Nutley, N.J. Its purity was not specified. The source and purity of methanol was not specified.
	ESTIMATED ERROR: Nothing specified
	REFERENCES: 1. *"The United States Pharmacopeia"*, 20th rev. U.S. Pharmacopeial Convention, Rockville, Md., 1980, p. 120.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) 2-Propanol; C_3H_8O; [67-63-0]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, 2, 467-86.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in 2-propanol at 25°C is 8.8 mg/ml (3.5×10^{-2} mol dm^{-3}, compiler). [a]

[a]The temperature and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with the solvent overnight at const temp (25°C) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken, weighed and the solvent removed in a vacuum oven. The wt of solute was detd after the residue had been dried to const wt. All weighing was done on a Mettler microbalance using microanal techniques.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. The solvent was purchased Reagent Grade and used without further purification.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)
Temp: not specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide,4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Ethanol, 2-ethoxy-; $C_4H_{10}O_2$; [110-80-5]	Sunwoo, C.; Eisen, H. *J. Pharm. Sci.*, 1971, *60*, 238-44.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

The mole fraction solubility of sulfamethoxazole in 2-ethoxyethanol at 25°C is 0.0911 (22.0 g/100 g solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Soly was detd by the method reported by Restaino and Martin. Sulfamethoxazole was assayed on a Coleman-Hitachi 124 double-beam spectrophotometer at 271 nm after diln of a sample with 95% alcohol or water.	Sulfamethoxazole (Hoffmann - La Roche, Inc., Nutley, N.J.) was recrystd from warm alcohol. 2-Ethoxyethanol (Cellosolve solvent, Union Carbide, New York, N.Y.) was of industrial grade.
	ESTIMATED ERROR: Soly: the mean of 3 runs was given (authors). Temp: ±1.0°C (authors).
	REFERENCES: 1. Restaino, F.A.; Martin, A.N. *J. Pharm. Sci.* 1964, *53*, 636.

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Ethanol; C_2H_6O; [64-17-5] (3) Methanol; CH_4O; [67-56-1]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, *2*, 467-86.
VARIABLES: One temperature: 25°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in 3A alcohol (ethanol containing approximately 5% methanol) at 25°C is 30.6 mg/ml (0.121 mol dm^{-3}, compiler).[a]

[a]The temperature, the composition of 3A alcohol and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
An excess of solute was equilibrated with the solvent overnight at const temp (25°) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken, weighed and the solvent removed in a vacuum oven. The wt of solute was detd after the residue had been dried to const wt. All weighing was done on a Mettler microbalance using microanal techniques.	The sulfamethoxazole was of reference standard quality equivalent to USP. The solvent was purchased Reagent Grade and used without further purification.
	ESTIMATED ERROR: Soly: precision ±1% (MacMullan) Temp: not specified
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Ethane, 1,1'-oxybis- (ethyl ether); $C_4H_{10}O$; [60-29-7]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, *2*, 467-86.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in ethyl ether at 25°C is 2.7 mg/ml (1.1×10^{-2} mol dm^{-3}, compiler).[a]

[a]The temperature and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with the solvent overnight at const temp (25°C) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken, weighed and the solvent removed in a vacuum oven. The wt of solute was detd after the residue had been dried to const wt. All weighing was done on a Mettler microbalance using microanal techniques.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. The solvent was purchased Reagent Grade and used without further purification.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)
Temp: not specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Petroleum ether; [8032-32-4]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, *2*, 467-86.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in petroleum ether (boiling range 30-60°C) at 25°C is 0.2 mg/ml (8×10^{-4} mol dm^{-3}, compiler). [a]

[a]The temperature and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with the solvent overnight at const temp (25°C) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken, weighed and the solvent removed in a vacuum oven. The wt of solute was detd after the residue had been dried to const wt. All weighing was done on a Mettler microbalance using microanal techniques.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. The solvent was purchased Reagent Grade and used without further purification.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)
Temp: not specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Benzene; C_6H_6; [71-43-2]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, *2*, 467-86.
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in benzene at 25°C is 0.5 mg/ml (2.0×10^{-3} mol dm^{-3}, compiler). [a]

[a]The temperature and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with benzene overnight at const temp (25°C) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken, weighed and the solvent removed in a vacuum oven. The wt of solute was detd after the residue had been dried to const wt. All weighing was done on a Mettler microbalance using microanal techniques.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. The solvent was purchased Reagent Grade and used without further purification.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)
Temp: not specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Benzene; C_6H_6; [71-43-2]	Takayama, K.; Nambu, N.; Nagai, T., *Chem. Pharm. Bull.* 1977, *25*, 2608-12.
VARIABLES:	**PREPARED BY:**
One temperature: 10°C	R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in benzene at 10°C is 3.60×10^{-4} mol dm^{-3} [a].

[a]Numerical value supplied by the authors.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The system was equilibrated in a sealed vial for 72 h at 10°C. The satd soln was rapidly filtered through a Toyo filter paper No. 5B, 1 cm^3 of the filtrate was evapd at 40°C and the residue was dissolved in $CHCl_3$ to det the concn in the UV region using a Hitachi 124 spectrophotometer.

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole, m.p. 167°C, was a very pure compd supplied by Shionogi Pharmaceutical Co., Ltd.

Purity of the benzene was not specified.

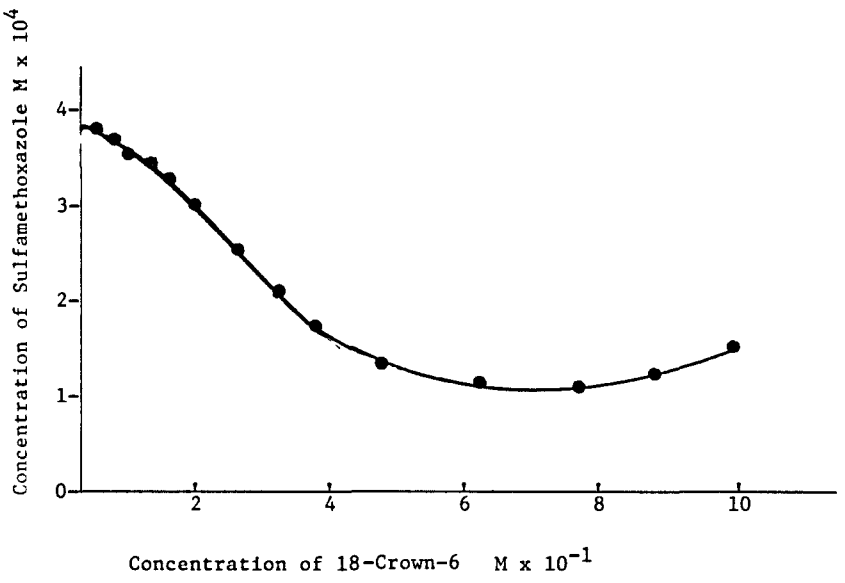
ESTIMATED ERROR:

None specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) 1,4,7,10,13,16-Hexaoxacyclooctadecane (18-Crown-6); $C_{12}H_{24}O_6$; [17455-13-9] (3) Benzene; C_6H_6; [71-43-2]	Takayama, K.; Nambu, N.; Nagai, T. *Chem. Pharm. Bull.* 1977, *25*, 2608-12.
VARIABLES: Concentration of 18-Crown-6	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:



AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
The system was equilibrated in a sealed vial for 72 h at 10°C. The satd. soln. was rapidly filtered through a Toyo filter paper No. 5B, 1 cm^3 of the filtrate was evapd. at 40°C and the residue was dissolved in $CHCl_3$ to det. the concn. in the UV region using a Hitachi 124 spectrophotometer.	Sulfamethoxazole, m.p. 167°C, was a very pure compd. supplied by Shionogi Pharmaceutical Co., Ltd. Purity of the benzene was not specified.
	ESTIMATED ERROR: None specified
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) 1,4,7,10,13,16-Hexaoxacyclooctadecane (18-Crown-6); $C_{12}H_{24}O_6$; [17455-13-9] (3) Benzene; C_6H_6; [71-43-2]	Takayama, K.; Nambu, N.; Nagai, T., *Chem. Pharm. Bull.* 1977, *25*, 2608-12.
VARIABLES: Concentration of 18-Crown-6	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Concentration of 18-Crown-6 10^3 mol dm^{-3}	Solubility at 10°C [a] 10^4 mol dm^{-3}
0.30	3.70
0.60	3.42
0.90	3.56
1.20	3.30
1.50	3.10
1.80	2.92
2.10	2.82
2.40	2.66
2.70	2.50
3.00	2.44
4.00	2.25
5.00	1.54
6.00	1.40
7.00	1.30
8.00	0.95
9.00	1.25
10.00	1.28

[a]Numerical values supplied by the authors

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

The system was equilibrated in a sealed vial for 72 h at 10°C. The satd soln was rapidly filtered through a Toyo filter paper No. 5B, 1 cm^3 of the filtrate was evapd at 40°C and the residue was dissolved in $CHCl_3$ to det the concn in the UV region using a Hitachi 124 spectrophotometer .

SOURCE AND PURITY OF MATERIALS:

Sulfamethoxazole, m.p. 167°C, was a very pure compd supplied by Shionogi Pharmaceutical Co., Ltd.

18-Crown-6 was of the reagent grade.

Purity of the benzene was not specified.

ESTIMATED ERROR:

None specified

REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]	Riess, W. *Intern. Congr. Chemotherapy, Proc., 3rd, Stuttgart* 1963, *1*, 627-32.
VARIABLES: One temperature: 20°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in chloroform at 20°C is 206 mg% (8.13×10^{-3} mol dm^{-3} solution, compiler).

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Nothing specified	Nothing specified
	ESTIMATED ERROR: Nothing specified
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfisomezole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Methane, trichloro- (chloroform); $CHCl_3$; [67-66-3]	Yamazaki, M.; Aoki, M.; Kamada, A.; Yata, N. *Yakuzaigaku*, 1967, *27(1)*, 37-40.
VARIABLES: One temperature: 30°C	PREPARED BY: R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfisomezole*in chloroform at 30°C is 6.75 mmol/L (1.71 g dm^{-3}, compiler).

* Another common trivial name is sulfamethoxazole.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
Sulfisomezole (0.5 g) was placed in an L-shaped tube together with 20 ml of chloroform. The mixt was shaken in a thermostat until equilibrium was attained. The sulfisomezole was assayed in the supernatant spectrophotometrically at 545 nm on a Beckmann DU spectrophotometer. The results were taken from a calibration graph.	Nothing specified
	ESTIMATED ERROR: Soly: not specified Temp: ±1°C (authors)
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6] (2) Methane, trichloro-; $CHCl_3$; [67-66-3]	Kitao, K.; Kubo, K.; Morishita, T.; Yata, N.; Kamada, A. *Chem. Pharm. Bull.* 1973, *21*, 2417-26.
VARIABLES: One temperature: 37°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in $CHCl_3$ at 37°C is 13.1 mmol dm^{-3} solution.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:	SOURCE AND PURITY OF MATERIALS:
One ml of the $CHCl_3$ soln of sulfamethoxazole at equilibrium was taken into a test tube. After evapn of the solvent, the residue was dissolved in 1N NaOH, the soln was properly dild with deionized water, and the concn of sulfamethoxazole was detd by diazotization.	Comm available sulfamethoxazole (source not specified) was used as supplied. Neither source nor the purity of the $CHCl_3$ was specified.
	ESTIMATED ERROR: Soly: not specified Temp: ±1°C (authors)
	REFERENCES:

COMPONENTS:	ORIGINAL MEASUREMENTS:
(1) Benzenesulfonamide, 4-amino-N-(5-methyl-3-isoxazolyl)- (sulfamethoxazole); $C_{10}H_{11}N_3O_3S$; [723-46-6]	Rudy, B.C.; Senkowski, B.Z. *Anal. Profiles Drug Subst.* 1973, *2*, 467-86.
(2) Methane, trichloro-; $CHCl_3$ [67-66-3]	
VARIABLES: One temperature: 25°C	**PREPARED BY:** R. Piekos

EXPERIMENTAL VALUES:

Solubility of sulfamethoxazole in trichloromethane at 25°C is 2.3 mg/ml (9.1×10^{-3} mol dm^{-3}, compiler). [a]

[a]The temperature and all auxiliary information was given by Edward A. MacMullan from Roche Products Inc., Manati, P.R., in a personal communication.

AUXILIARY INFORMATION

METHOD/APPARATUS/PROCEDURE:

An excess of solute was equilibrated with trichloromethane overnight at const temp (25°C) while being agitated with a 60 cycle vibrator (VIBROMIXER). A portion of the clear supernatant soln was then taken, weighed and the solvent removed in a vacuum oven. The wt of solute was detd after the residue had been dried to const wt. All weighing was done on a Mettler microbalance using microanal techniques.

SOURCE AND PURITY OF MATERIALS:

The sulfamethoxazole was of reference standard quality equivalent to USP. The solvent was purchased Reagent Grade and used without further purification.

ESTIMATED ERROR:

Soly: precision ±1% (MacMullan)

Temp: not specified

REFERENCES: