

A Systematic Method Development Strategy for Determination of Pharmaceutical Genotoxic Impurities

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Derivatization reaction of DMS with 2-mercaptopyridine:

Standard solution of dimethyl sulfate (DMS) is prepared at about 0.0025 mg /mL after serial dilution, corresponding to 0.1% (w/w) relative to a 2.5 mg/mL sample (starting material) in case study 4.

Derivatization reagent is an aqueous solution of 5 mg/mL 2-mercaptopyridine prepared by dissolving 50 mg of 2-mercaptopyridine in 10 mL of water followed by sonication for 5 minutes. Starting material samples are prepared in duplicate at a concentration of 2.5 mg/mL in acetonitrile. Spike recovery samples are prepared by dissolving 2.5 mg/ml starting material in the standard solution.

Transfer 5 mL of standard solutions, samples, and spike recovery samples into 9-mL vials respectively, to which 1 mL of derivatization reagent solution was added. Mix well and transfer 1 mL of the solutions into 2-mL HPLC vials respectively. The resulting vials are heated on a heating block at 60 °C for 60 minutes before subjecting to HPLC analysis.