

Development of a General Solvents Method for DMSO Soluble Compounds
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Organic solvents are used in the synthesis of active pharmaceutical ingredients and drug products. However, the solvent itself has no therapeutic value. Therefore one goal in developing pharmaceutical processes is to remove and control the solvent content to levels that are acceptable from a toxicological perspective for patient safety. Solvents that are used to manufacture drug substances and drug products are not unique to a project or process. A list of 29 potential solvents preferred or commonly used in manufacturing was compiled.

Methodology to control and determine the level of residual solvent has been developed based on modifications of the USP<467> and Ph.Eur. 2.4.24 methods. Pro ezGC™ development software was utilized to aid in the evaluation of the chromatographic conditions to optimize both the resolution of the analytes and the analysis time. The general solvent method has been validated for the 29 solvents over the range of 10% to 200% of the target limit for the individual solvents. The method developed provides for the quantitative determination of the various solvents in DMSO soluble compounds by standard addition using headspace GC. Method development and use, the advantages and limitations, and a comparison to the USP<467> method will be discussed.