# RESIDUAL SOLVENTS – USP<467>

Quantex Laboratories provides comprehensive testing to meet the need of complying with the requirements of the USP <467> Residual Solvents. On July 1, 2008, the USP implemented a new test requirement for the control of residual solvents in drug products. The new test requirement, USP General Chapter <467> Residual Solvents, replaces the previous USP General Chapter <467> Organic Volatile Impurities. This new test requirement is more comprehensive, as it increases the number of residual solvents to be routinely tested to 57. This is a much longer analyte list than previously tested and represents the sum of Class 1, 2 and 3 residual solvents. Class 1 compounds are carcinogenic, posing a risk to both the consumer and the environment. Class 2 compounds are non-genotoxic animal carcinogens, with concentrations of these compounds to be limited. Class 3 compounds, have low toxic potential. Testing should be performed for those residual solvents that are used or produced in the manufacture or purification of drug substances, excipients or drug products. For finished product, you may choose to test either all the individual components- raw materials, API, excipients or the final finished product.

**What's required…**

The new test requirement itself is also more extensive and divided into three distinct procedures (A, B and C) for identification, confirmation, and quantification. The new test requirement for residual solvents under USP <467> consists of static headspace extraction followed by gas chromatographic separation and flame ionization detection (HS-GC/FID). Headspace sample preparation is also divided into two separate sections based upon sample solubility: water soluble and water insoluble articles. Procedure A is the first step in the identification process and is performed on a G43 capillary column as a means of determining if any residual solvents are present in the sample at detectable levels. If no residual solvent peaks are larger than the standard, then the testing would be done.

If, however, a residual solvent is identified above the percent daily exposure limit, Procedure B is then performed to confirm analyte identity using a G16 capillary column. Once identity is confirmed, Procedure C then uses the conditions which yielded the best or most favorable separation- Procedure A or B- to provide a quantifiable result. If only Class 3 solvents are employed, their level is determined by USP method <731> Loss on Drying and if their contribution is greater than 0.5%, further testing for moisture content is required by USP method <921> .

Be aware that where suitable chromatography cannot be obtained due to sample matrix interference, method development may be required. Unknown peaks in test samples may also require further analysis , which is at your discretion. The USP has stated that a company does have the option to develop and validate their own internal method for determining residual solvents rather than using the USP Residual Solvents <467> method.

**USP Residual Solvents method <467> has radically changed (July 2008) and there are now 57 solvents listed as either Class 1, Class 2 or Class 3 This new procedure now requires a different approach (similar to the current EP methods):**

- Preliminary GC screening (Procedure A)
- Confirmatory analysis using dissimilar column chemistry (Procedure B)
- Identification of any solvent identified under both analyses above
- Quantitative analysis (Procedure C)

**We offer expert service for the analysis of residual solvents which includes:**

- Headspace GC-FID
  Identification and quantitation Per USP <467>
- GC-MS Screen using alternative selectivity columns (with Headspace or Thermal Desorption)
- Expert spectral interpretation where required
- Method development & validation as needed
- Technical Transfer of the method

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For more information on our capabilities please contact our Business Development group at (609) 655-4047, extension 304.

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