RESIDUAL SOLVENTS USP <467>

Residual solvents, previously referred to as organic volatile impurities (OVIs), are trace level chemical residues that are used or produced in the manufacture of drug substances and excipients or in the preparation of drug products. They can also be by-products formed during packaging and storage of the drug product.

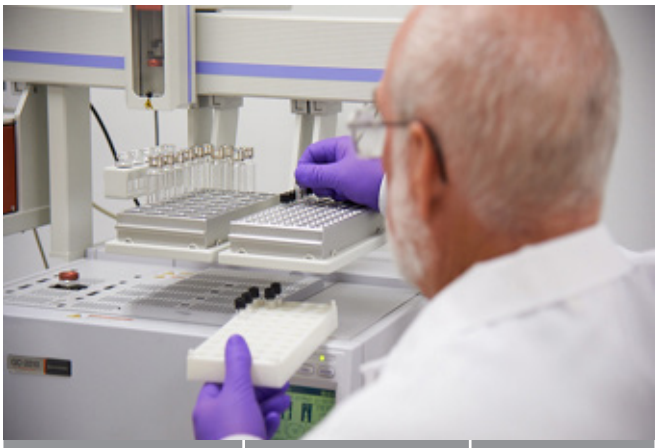
The United States Pharmacopeia general chapter on residual solvent analysis, USP <467>, corresponds to the International Conference on Harmonization (ICH) guideline Q3C (R4). The guideline recommends acceptable levels of residual solvents in pharmaceutical products to ensure patient safety. Analytical testing of drug substances, excipients and final products should be performed when production or purification processes are known to result in the presence of residual solvents.

Residual solvents are separated into three classes related to their potential toxicity. Class 1 solvents are generally avoided in pharmceutical manufacturing, because they are known carcinogens, strongly suspected carcinogens, or environmental hazards. Class 2 solvents are limited use solvents that are nongenotoxic animal carcinogens or possible agents of other irreversible toxicity such as neurotoxicity or teratogenicity. Class 3 solvents have low toxic potential to humans where no health-based exposure limit is needed. Procedures are presented for establishing exposure limits. Ingredent and product specifications are required and testing is needed to satisfy current Good Manufacturing Practices. Manufacturers may test the drug product or use a cumulative method to calculate the residual solvent levels in the drug product based on levels in the ingredients used to produce the product.

The analytical procedure in USP <467> consists of a static headspace extraction coupled with a gas chromatographic separation and flame ionization detection (GC/FID). The procedure utilized is based on the water solubility of the material being tested. The test method consists of three separate procedures that are designed to identify, confirm and quantify residual solvents in pharmaceuticals.

R. D. Laboratories, Inc. is uniquely qualified to assist you with your residual solvent testing needs. Implementing USP <467> requires specialized equipment with careful selection of chromatographic supplies and operating parameters. Our analysts have extensive experience in optimizing gas chromatographic methods and analyzing volatile organic compounds in a variety of matrices.

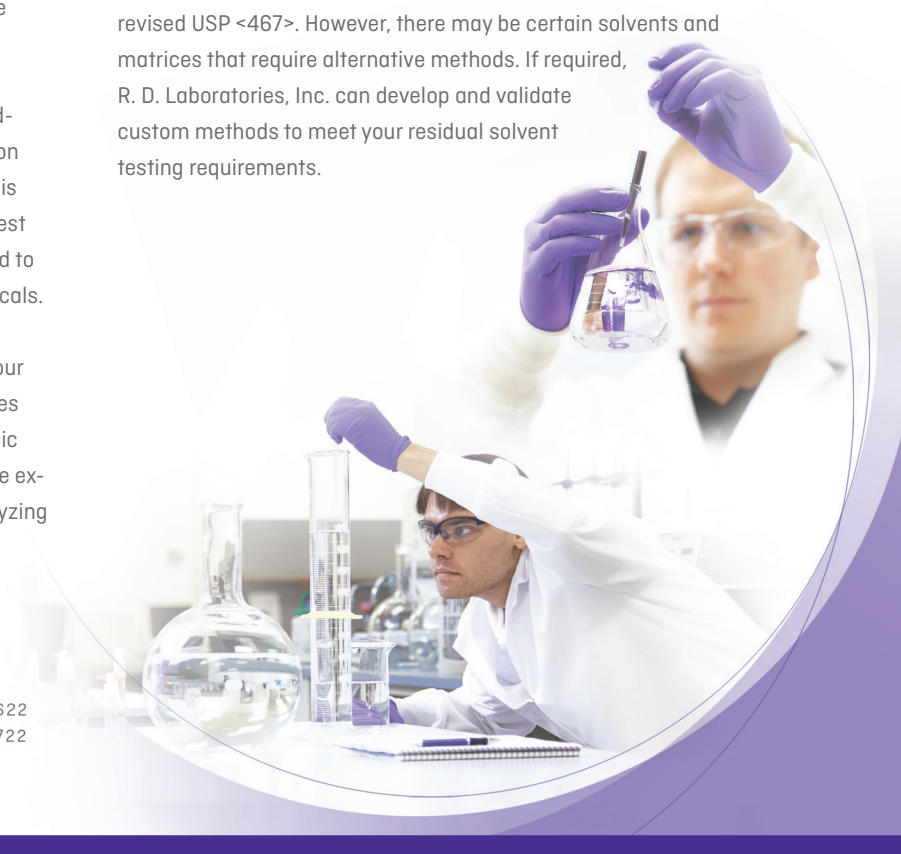
R. D. Laboratories, Inc, has multiple gas chromatographs with a variety of injection and detection techniques.



Gas Chromatographs	Detectors	Capabilities
Shimadzu	Flame Ionization	Capillary Column
GC-14A, GC-17A,	Thermal Conductivity	Packed Colum
GC-2010, GC-2014,		Direct Injection
GC-2010		Headspace

All equipment has been fully validated (IQ/OQ/PQ) and system suiability is performed using traceable reference standard residual solvent solutions to satisfy current Good Manufacturing Practice regulations.

The majority of the solvents specified can be analyzed using the revised USP <467>. However, there may be certain solvents and matrices that require alternative methods. If required, R. D. Laboratories, Inc. can develop and validate custom methods to meet your residual solvent testing requirements.



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