STREAMLINE YOUR
USP <467> RESIDUAL SOLVENT DETECTION

The Measure of Confidence

Agilent Residual Solvent Analyzers

The manufacturing process of active pharmaceutical ingredients (APIs) may contribute to residual solvents remaining in the final pharmaceutical product. Producers need to monitor and control the levels of residual solvents for a number of reasons including safety, effect on crystalline form, solubility, bioavailability, and stability. All drug substances, excipients, and products must conform to strict regulatory limits.

Consistently analyze residual solvents immediately following installation

Agilent Residual Solvent Analyzers are based on the Agilent 7890B GC system – and are factory pre-tested and pre-configured to deliver the results you need, *fast*, while saving you precious start-up time. What's more, their analytical precision exceeds USP method requirements for the three classes of residual solvents:

Class 1: Solvents to be avoided
- Known human carcinogens
- Strongly suspected human carcinogens
- Environmental hazards

Class 2: Solvents to be limited
- Nongenotoxic animal carcinogens, or possible agents that cause irreversible toxicity
- Solvents suspected of significant, but reversible, toxicity

Class 3: Solvents with low toxic potential
- No health-based exposure limits

The Analyzer's inert sample path and thermal zone stability – combined with the automation capabilities of the Agilent 7697A Headspace Sampler – provide unsurpassed accuracy and repeatability.

Agilent Residual Solvent Analyzers reflect innovative technology and a stringent quality control process. Systems include:

Factory
- System assembly, performance check, and leak testing
- Application configuration, installation of appropriate columns and accessories
- Factory chemical performance verification with application-specific chemical checkout mix

Delivery
- CD-ROM with method parameters and checkout data files for easy out-of-the-box operation
- Instrument and method operational manuals
- Application-related consumables – no separate ordering required
- Information to help you reorder consumables easily

Installation
- Onsite installation by factory-certified support engineer
- Duplicate factory checkout with application-specific checkout sample
- Optional application startup assistance

GC/FID/MS
Residual Solvent Analyzer

GC/FID & GC/FID/FID
Residual Solvent Analyzers

Agilent Technologies

Facilitate your QA/QC with Agilent USP <467> Residual Solvent Analyzers

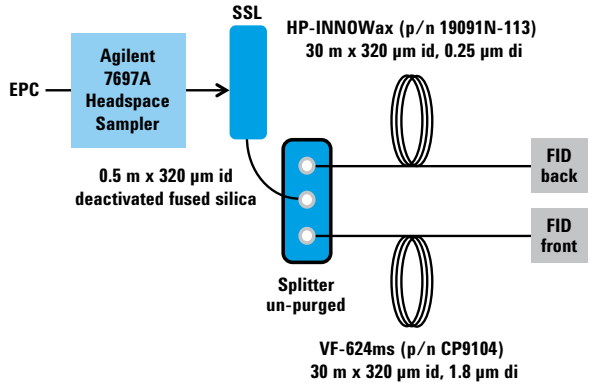
- Pre-configured to meet system suitability requirements for USP <467>, including column, consumables, calibration/checkout samples, and analytical method
- Chemically tested to ensure optimal analysis of Class 1 and Class 2A/B solvents
- With precise temperature and sampling control routines, the Agilent 7697A Headspace Sampler maximizes throughput and minimizes operator error
- Headspace thermal zone stability of ±0.1 °C, inert flow path, and patented Capillary Flow Technology (CFT) provide excellent RSD for USP Class 1A and Class 2A/B solvents while minimizing carryover
- Begin system calibration and validation immediately following installation
- **Choose from two configurations:**
  - **GC/FID (or GC/FID/FID)** couples an Agilent 7697A Headspace Sampler with an Agilent 7890B GC. The configuration uses either one or two columns.
  - **GC/FID/MS** joins the Agilent 7697A Headspace Sampler with an Agilent 5977 Series GC/MSD system.

GC/FID and GC/FID/FID Residual Solvent Analyzers

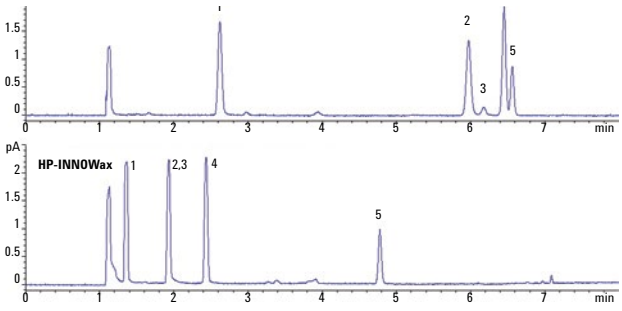
Easily quantitate OVI content

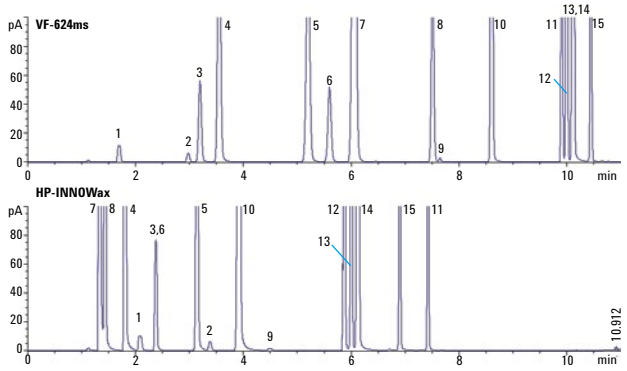
Agilent GC/FID Analyzers are ideal for identifying organic contaminants in active ingredients, formulations, and additives. Single-channel systems provide easy OVI quantitation, while the dual-FID configuration uses dissimilar columns for additional confirmation within a single injection

GC/FID/FID Configuration



	Identity	USP limit (ppm)	RSD (%)
Class 1			
1	1,1-Dichloroethene	8	2.3
2	1,1,1-Trichloroethane	1,500	1.7
3	Carbon tetrachloride	4	1.9
4	Benzene	2	1.7
5	1,2-Dichloroethane	5	2.1
Class 2A			
1	Methanol	3,000	0.8
2	Acetonitrile	410	0.8
3	Dichloromethane	600	0.3
4	*trans*-1,2-Dichloroethene	1,870	0.8
5	*cis*-1,2-Dichloroethene	1,870	1.4
6	Tetrahydrofuran	720	1.1
7	Cyclohexane	3,880	1.4
8	Methylcyclohexane	1,180	1.5
9	1,4-Dioxane	380	1.4
10	Toluene	890	1.7
11	Chlorobenzene	360	0.4
12	Ethylbenzene	2,170	0.6
13, 14	*m*-Xylene, *p*-Xylene,	2,170	2.2
15	*o*-Xylene	2,170	2.2
Class 2B			
1	Hexane	290	3.1
2	Nitromethane	50	4.3
3	Chloroform	60	1.7
4	1,2-Dimethoxyethane	100	1.5
5	Trichloroethene	80	2.0
6	Pyridine	200	1.4
7	2-Hexanone	50	1.6
8	Tetralin	100	1.7





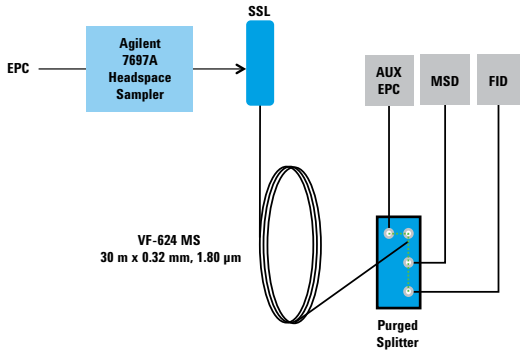
Here, excellent results were obtained at USP <467> specified limit concentrations for all three classes of residual solvents. (Peaks are identified in the table above.)

GC/FID/MS Residual Solvent Analyzers

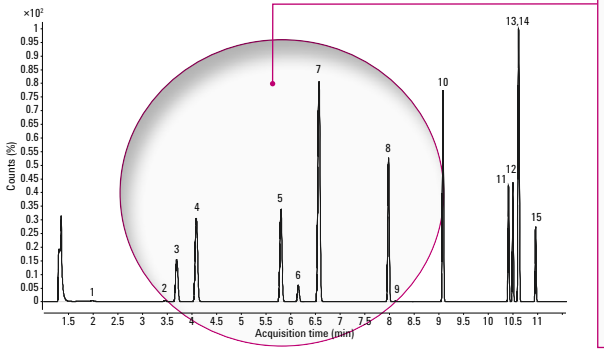
Perform confident quantitation and MS confirmation

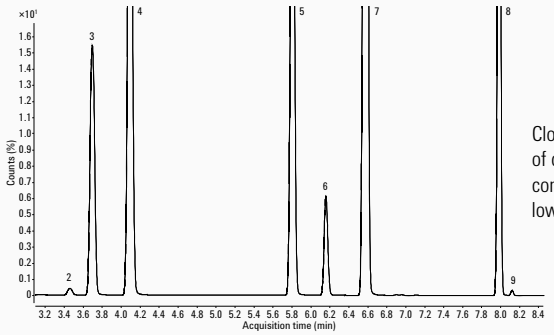
Quantify and spectrally confirm unknown organic contaminants in pharmaceutically active ingredients, formulations, and additives with GC/FID/MS analysis.

GC/FID/MS Configuration



	Identity	USP limit (ppm)	Scan RSD (%)	SIM RSD (%)
Class 1	n = 8			
1	1,1-Dichloroethene	8	09	
2	1,1,1-Trichloroethane	1,500	19	
3	Carbon tetrachloride	4	15	
4	Benzene	2	07	
5	1,2-Dichloroethane	5	09	
Class 2A	n = 10			
1	Methanol	3,000	28	2.4
2	Acetonitrile	410	33	2.3
3	Dichloromethane	600	25	2.2
4	*trans*-1,2-Dichloroethene	1,870	24	2.2
5	*cis*-1,2-Dichloroethene	1,870	21	2.1
6	Tetrahydrofuran	720	30	2.2
7	Cyclohexane	3,880	27	1.3
8	Methylcyclohexane	1,180	43	1.6
9	1,4-Dioxane	380	26	2.3
10	Toluene	890	07	2.0
11	Chlorobenzene	360	19	2.1
12	Ethylbenzene	2,170	19	2.1
13, 14	*m*-Xylene, *p*-Xylene,	2,170	21	1.8
15	*o*-Xylene	2,170	21	1.8
Class 2B	n = 9			
1	Hexane	290	32	
2	Nitromethane	50	38	
3	Chloroform	60	25	
4	1,2-Dimethoxyethane	100	27	
5	Trichloroethene	80	25	
6	Pyridine	200	39	
7	2-Hexanone	50	24	
8	Tetralin	100	25	





Close-up view of data, showing compounds with low response.

Outstanding repeatability for analyzing residual solvents. For QA labs, the MSD configuration is particularity useful for unknown identification, or for unambiguous confirmation. (SIM/Scan data appear in the table above.)

Residual Solvent Analyzers for quantitating and confirming OVIs in APIs

Description	P/N	Sample Types	Target Analytes
USP <467> Residual Solvent Analyzer HSS/GC/FID/MSD Used for QA/QC for quantitation of residuals and identification of unknowns.	G3445B#481	• Active pharmaceutical ingredients (APIs) • Pharmaceutical formulations	**Class 1 Solvents** (1,1-dichloroethene, 1,1,1-trichloroethane, Carbon tetrachloride, Benzene, 1,2-dichloroethane) **Class 2A Solvents** (Methanol, Acetonitrile, Dichloromethane, Trans 1,2-dicloroethene, Cis 1,2-dichloroethene, Tetrahyrofuran, Cyclohexene, Methylcyclohexane, 1,4-dioxane, Toluene, Chlorobenzene, Ethylbenzene, o,m,p-xylene) **Class 2B Solvents** (Hexane, Nitromethane, Chloroform, 1,2-dimethoxyethane, Trichloroethene, Pyridine, 2-hexanone, Tetralin)
USP <467> Residual Solvent Analyzer HSS/GC/FID Provides quick screening for residual organic contaminants.	G3445B#681	• Active pharmaceutical ingredients (APIs) • Pharmaceutical formulations	**Class 1 Solvents** (1,1-dichloroethene, 1,1,1-trichloroethane, Carbon tetrachloride, Benzene, 1,2-dichloroethane) **Class 2A Solvents** (Methanol, Acetonitrile, Dichloromethane, Trans 1,2-dicloroethene, Cis 1,2-dichloroethene, Tetrahyrofuran, Cyclohexene, Methylcyclohexane, 1,4-dioxane, Toluene, Chlorobenzene, Ethylbenzene, o,m,p-xylene) **Class 2B Solvents** (Hexane, Nitromethane, Chloroform, 1,2-dimethoxyethane, Trichloroethene, Pyridine, 2-hexanone, Tetralin)
USP <467> Residual Solvent Analyzer HSS/GC/FID/FID) Dissimilar columns provide quantitation and confirmation in a single injection.	G3445B#682	• Active pharmaceutical ingredients (APIs) • Pharmaceutical formulations	**Class 1 Solvents** (1,1-dichloroethene, 1,1,1-trichloroethane, Carbon tetrachloride, Benzene, 1,2-dichloroethane) **Class 2A Solvents** (Methanol, Acetonitrile, Dichloromethane, Trans 1,2-dicloroethene, Cis 1,2-dichloroethene, Tetrahyrofuran, Cyclohexene, Methylcyclohexane, 1,4-dioxane, Toluene, Chlorobenzene, Ethylbenzene, o,m,p-xylene) **Class 2B Solvents** (Hexane, Nitromethane, Chloroform, 1,2-dimethoxyethane, Trichloroethene, Pyridine, 2-hexanone, Tetralin)

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- Trouble-free instrument operation
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Custom GC and GC/MS configurations

Let Agilent customize a standard GC or GC/MS Analyzer with specialized columns, valves, tubing inlets, and other add-ons – including an extensive line of consumables and column modules.

Ordering information:

- USP <467> Residual Solvent Analyzer (HSS/GC/FID/MSD): G3445B#481
- USP <467> Residual Solvent Analyzer (HSS/GC/FID): G3445B#681
- USP <467> Residual Solvent Analyzer (HSS/GC/FID/FID): G3445B#682

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