Scharlau

The wise choice

Solvents for GC-Headspace

Volatile residues under control

Analysis of residual solvents

The pharmaceutical industry shall guarantee that its products are free from impurities that could cause harmful effects in consumers.
In order to do this, analysis of residual solvents is necessary both in raw materials and in finished products.

Headspace gas chromatography is the comprehensive control procedure for analyzing and quantifying volatile organic solvents in a wide variety of samples.
Solvents employed for such application should have strictly controlled levels of residual volatile solvents, since they could interfere in the sample analysis.

The ICH Q3C guideline and the United States and European Pharmacopoeias (USP Chapter <467> and Ph Eur chapter 2.4.24 methods) have established the maximum allowed residual solvent limits. Both pharmacopoeias agree either the limits and the classification of residual solvents into three groups (see Tables 1, 2 and 3), according to the risk they pose to human health.

Maximum limits accepted by ICH Guideline

Table 1.
Class 1 solvents: should be avoided in pharmaceutical products

Solvent	Concern	Concentration limit (ppm)
Benzene	Carcinogen	2
Carbon tetrachloride	Toxic and environmental hazard	4
1,2-Dichloroethane	Toxic	5
1,1-Dichloroethene	Toxic	8
1,1,1-Trichloroethane	Environmental hazard	1.500

Table 2.
Class 2 solvents: should be limited in pharmaceutical products

Solvent	PDE* (mg/day)	Concentration limit (ppm)
Acetonitrile	4,1	410
Chlorobenzene	3,6	360
Chloroform	0,6	60
Cyclohexane	38,8	3.880
Cumene	0,7	70
1,2-Dichloroethene	18,7	1.870
Dichloromethane	6	600
1,2-Dimethoxyethane	1	100
N,N-Dimethylacetamide	10,9	1.090
N,N-Dimethylformamide	8,8	880
1,4-Dioxane	3,8	380
2-Ethoxyethanol	1,6	160
Ethylene glycol	6,2	620
Formamide	2,2	220
Hexane	2,9	290
Methanol	30	3.000
2-Methoxyethanol	0,5	50
Methyl butyl ketone	0,5	50
Methylcyclohexane	11,8	1.180
Methyl isobutyl ketone	45	4500
N-Methylpyrrolidone	5,3	530
Nitromethane	0,5	50
Pyridine	2	200
Sulfolane	1,6	160
Tetrahydrofuran	7,2	720
Tetralin	1	100
Toluene	8,9	890
1,1,2-Trichloroethene	0,8	80
Xylene (isomers)	21,7	2.170

*Permitted daily exposure.

Table 3.
Class 3 solvents: with low risk to human health

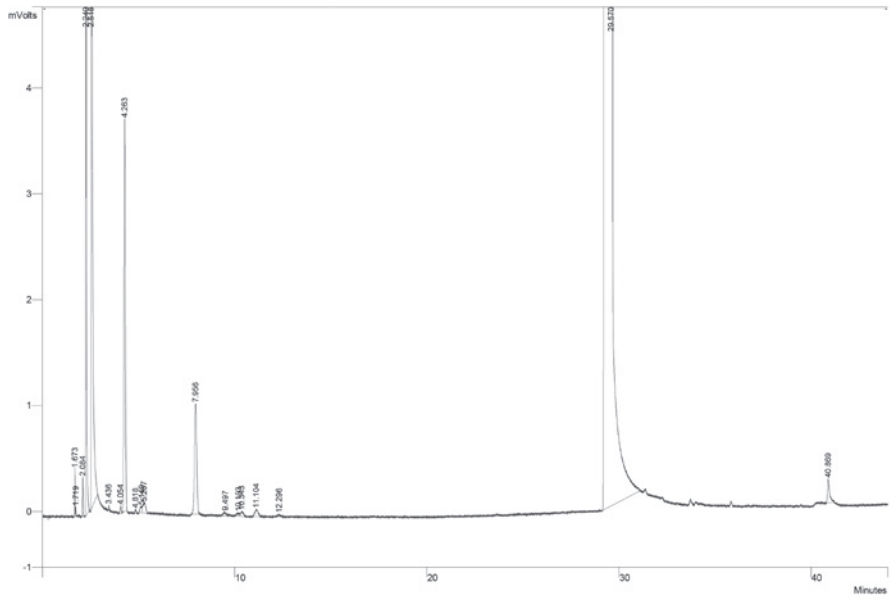
Solvent	Concentration limit (ppm)
Acetic acid	50 mg per day (5.000ppm)
Acetone	
Anisole	
1-Butanol	
2-Butanol	
n-Butyl acetate	
tert-Butyl methyl ether	
Dimethyl sulfoxide	
Ethanol	
Ethyl acetate	
Ethyl ether	
Ethyl formate	
Formic acid	
Heptane	
Isobutyl acetate	
Isopropyl acetate	
Methyl acetate	
3-Methyl-1-butanol	
Methyl ethyl ketone	
2-Methyl-1-propanol	
Pentane	
1-Pentanol	
1-Propanol	
2-Propanol	
n-Propyl acetate	
Triethylamine	

GC-Headspace Scharlau products

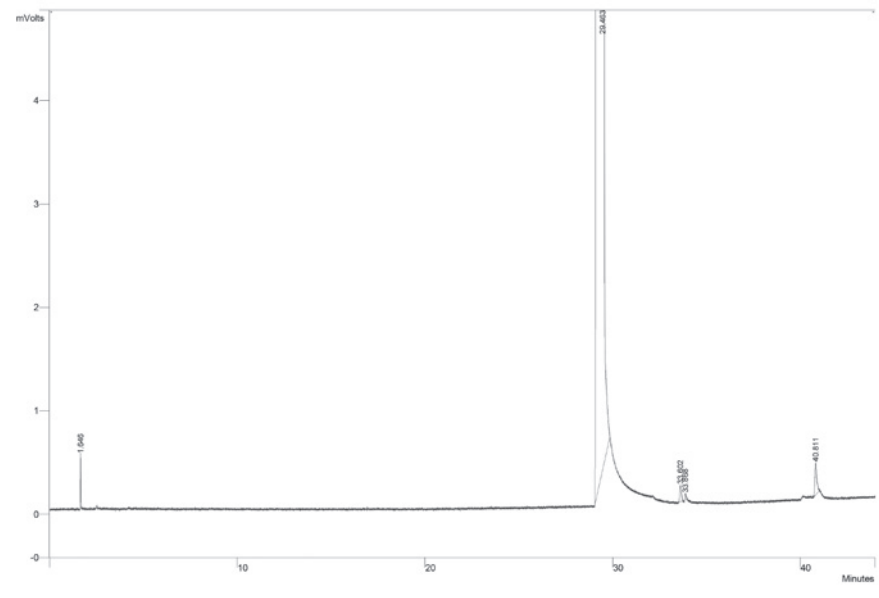
Scharlau GC-Headspace solvents are under purification processes to eliminate volatile impurities that could interfere in GC-Headspace analyses.
The bottling procedure is also critical in keeping purified products away from traces of residual solvents in the atmosphere which may cause contamination.
The final product is a solvent optimized for the analysis of residual solvents by GC-Headspace, assuring reproducible and accurate results in every analysis.

Figure 1.
Commonly reagent grade solvents are used in GC procedures, but GC-Headspace requires a quality with controlled levels of residual solvents.

DMF, reagent grade



DMF, GC-Headspace grade



Chromatographic conditions

- Column: 30m x 0,53mm x 3µm, silica (6% cyanopropylphenyl)
- Temperature program: 40°C (20 min), increasing rate 5°C/min until 160°C
- Injector: 200°C
- Detector: 300°C, FID
- Carrier gas: Helium
- Constant column flow: 4.0ml/min
- Split ratio: 50
- Hydrogen flow: 30ml/min
- Air flow: 300ml/min
- Make up flow: 26ml/min

Headspace conditions

- Oven temperature: 80°C
- Loop temperature: 90°C
- Transfer line temperature: 90°C
- Equilibration time: 50 min, with shaking
- Inject time: 1 min
- Sample volume (in vial): 10,0ml
- Injection volume: 1ml

GC-Headspace Quality

✓ Performance test on every batch

Each batch is controlled in our QC laboratory by means of GC-Headspace to ensure its suitability for the analysis of residual solvents.

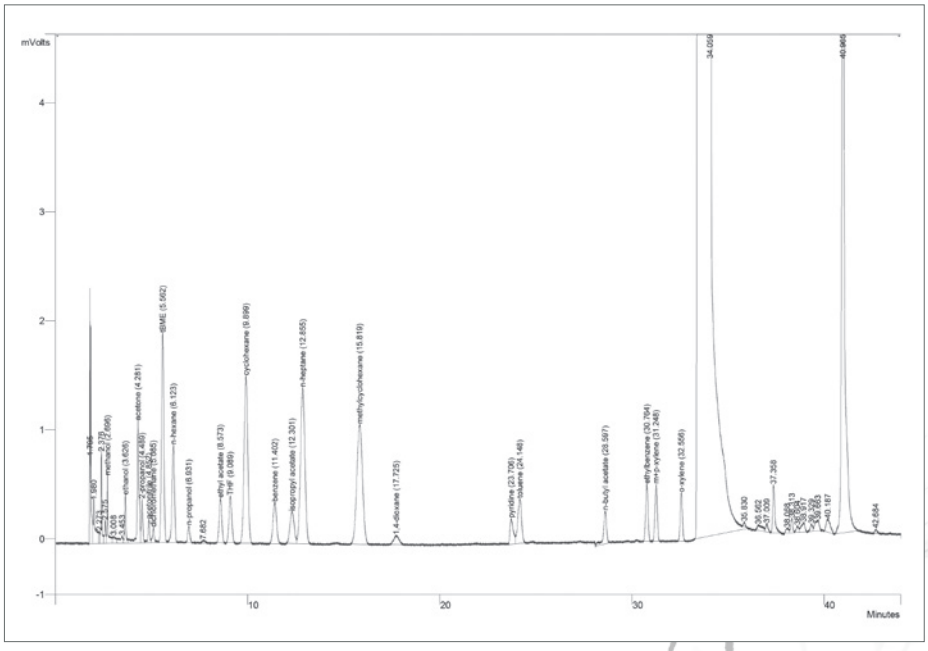
✓ Specified concentration of residual solvents

The values of solvent traces, if present, are stated in the certificate of analysis.

Table 4.
Maximum limits of residual solvents contained in our solvents for GC-Headspace:

Residual solvents	(mg/l)
Acetone	1
Acetonitrile	0,4
Benzene	0
n-Butanol	1
n-Butyl acetate	1
Cyclohexane	1
Dichloromethane	0,6
1,4-Dioxane	0,4
Ethanol	1
Ethyl acetate	1
Ethylbenzene	1
n-Heptane	1
n-Hexane	0,3
Isopropyl acetate	1
Methanol	1
Methylcyclohexane	1
Pyridine	1
2-Propanol	1
n-Propanol	1
tBME	1
THF	0,7
Toluene	0,9
m-Xylene	1
o-Xylene	1
p-Xylene	1

Figure 2.
As the GC-Headspace technique requires pressurization of the vial for sampling, and environmental pressure varies each day, the retention times are affected and may even vary. Therefore, a standard mixture is injected on regular basis.



Ordering information

Product	Art. No.	Capacity
N,N-Dimethylacetamide, for GC-HS	DI08621000	1 L
N,N-Dimethylformamide, for GC-HS	DI10741000	1 L
Dimethylsulfoxide, for GC-HS	SU01651000	1 L
N-Methyl-2-Pyrrolidone, for GC-HS	ME05031000	1 L
Water, for GC-HS	AG00141000	1 L

Visit our website for additional information
of our complete range of GC-Headspace products

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