PanReac AppliChem
ITW Reagents

infoPoint

Solvents for GC-Headspace

During the manufacturing of actives or excipients, or during the preparation of medicinal products, solvents that are used may not be completely removed. These solvents may have harmful effects on human health or on the environment and must be removed to the maximum extent possible. ICH's Q3C guide (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) establishes the acceptable levels of residual solvents in pharmaceuticals and classifies them according to their toxicity (see class 1, 2 and 3 solvents lists on the back).

It also describes the official methods for content analysis of said solvents in actives, excipients and/or medicines. The European Pharmacopoeia and the USP have adopted these same guidelines (Ph. Eur. method 2.4.24 and USP <467>).

The method normally consists of dissolving the sample in an appropriate solvent (water, dimethyl sulfoxide or dimethyl formamide, among others) to remove the residual solvent. Subsequent analysis is done by Headspace Gas Chromatography.

Therefore it is important that the solvent to be used for dissolving the sample has maximum purity and contains none of the residual solvents to be analyzed.

At PanReac AppliChem we are experts on solvent purification and control; we offer three of the most frequently used solvents in the preparation of samples for subsequent analysis by Headspace Gas Chromatography.

To ensure the utmost quality of these new solvents it has been necessary to develop new, more demanding manufacturing and packaging protocols.

Product	Assay (min.)	Code	Pack.
N,N-Dimethylacetamide	99,9 %	753145.1611	1000 ml
		753145.1612	2,5 L
N,N-Dimethylformamide	99,9 %	751785.1611	1000 ml
		751785.1612	2,5 L
Dimethyl Sulfoxide	99,9 %	751954.1611	1000 ml
		751954.1612	2,5 L

According to their risk to human health, residual solvents have been grouped into 3 categories:

Class 1: Solvents that should be avoided.
Class 2: Solvents to be limited.
Class 3: Solvents with low toxic potential.

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In the following lists, solvents classified into the 3 categories show their permitted limit concentrations. The concentrations typically found of residual solvents in our **GC-Headspace grade solvents** are less than **0.5 ppm** for class 1, less than **5 ppm** for class 2 and less than **25 ppm** for class 3.

Class 1: Solvents that should be avoided.

	Concentration limit (ppm)
Benzene	2
Carbon Tetrachloride	4
1,2-Dichloroethane	5
1,1-Dichloroethene	8
1,1,1-Trichloroethane	1500

Class 3: Solvents with low toxic potential

Concentration limit 5000 ppm

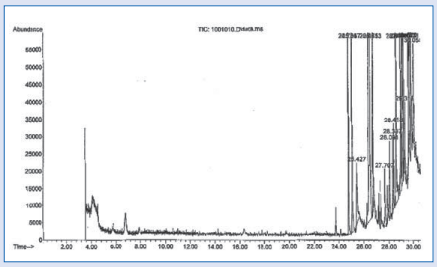
Acetic acid	Ethanol	3-Methyl-1-butanol
Acetone	Ethyl acetate	Methylethylketone
Anisole	Ethyl ether	Methylisobutylketone
1-Butanol	Ethyl formate	2-Methyl-1-propanol
2-Butanol	Formic acid	Pentane
Butyl acetate	Heptane	1-Pentanol
tert-Butylmethyl ether	Isobutyl acetate	1-Propanol
Cumene	Isopropyl acetate	2-Propanol
Dimethyl sulfoxide	Methyl acetate	Propyl acetate

Class 2: Solvents to be limited

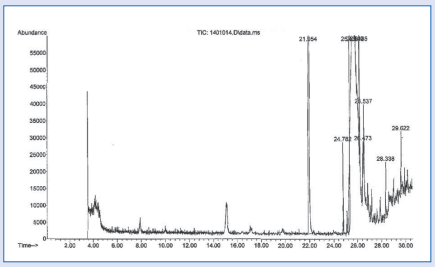
	Concentration limit (ppm)
Acetonitrile	410
Chlorobenzene	360
Chloroform	60
Cyclohexane	3880
1,2-Dichloroethene	1870
Methylene chloride	600
1,2-Dimethoxyethane	100
N,N-Dimethylacetamide	1090
N,N-Dimethylformamide	880
1,4-Dioxane	380
2-Ethoxyethanol	160
Ethyleneglycol	620
Formamide	220
Hexane	290
Methanol	3000
2-Methoxyethanol	50
Methylbutylketone	50
Methylcyclohexane	1180
N-Methylpyrrolidone	530
Nitromethane	50
Pyridine	200
Sulfolane	160
Tetrahydrofuran	720
Tetralin	100
Toluene	890
Trichloroethylene	80
Xylene	2170

See below the chromatograms obtained for PanReac AppliChem **HPLC-grade** dimethyl sulfoxide (DMSO), N,N-dimethyl formamide (DMF) and N,N-dimethyl acetamide (DMA) **compared to the GC-Headspace** grade solvents.

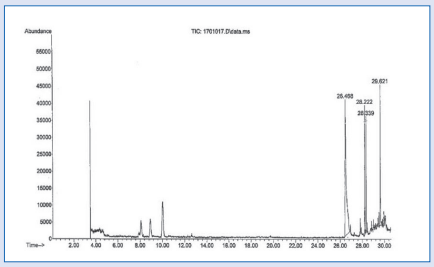
DMSO for UV, IR, HPLC, GPC (code 361954)



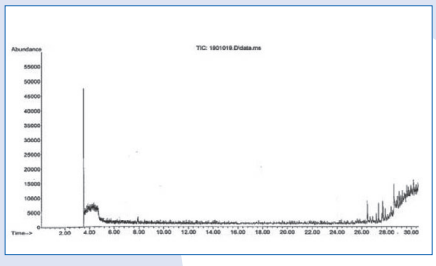
DMF for UV, IR, HPLC, GPC, ACS (code 361785)



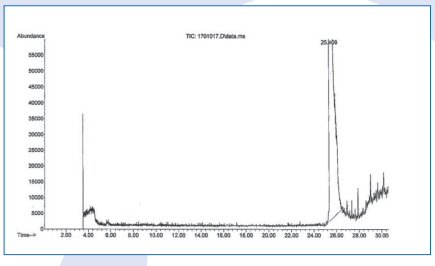
DMA for UV, IR, HPLC (code 363145)



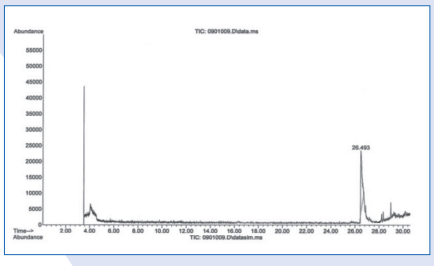
DMSO for Headspace GC (code 751954)



DMF for Headspace GC (code 751785)



DMA for Headspace GC (code 753145)



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