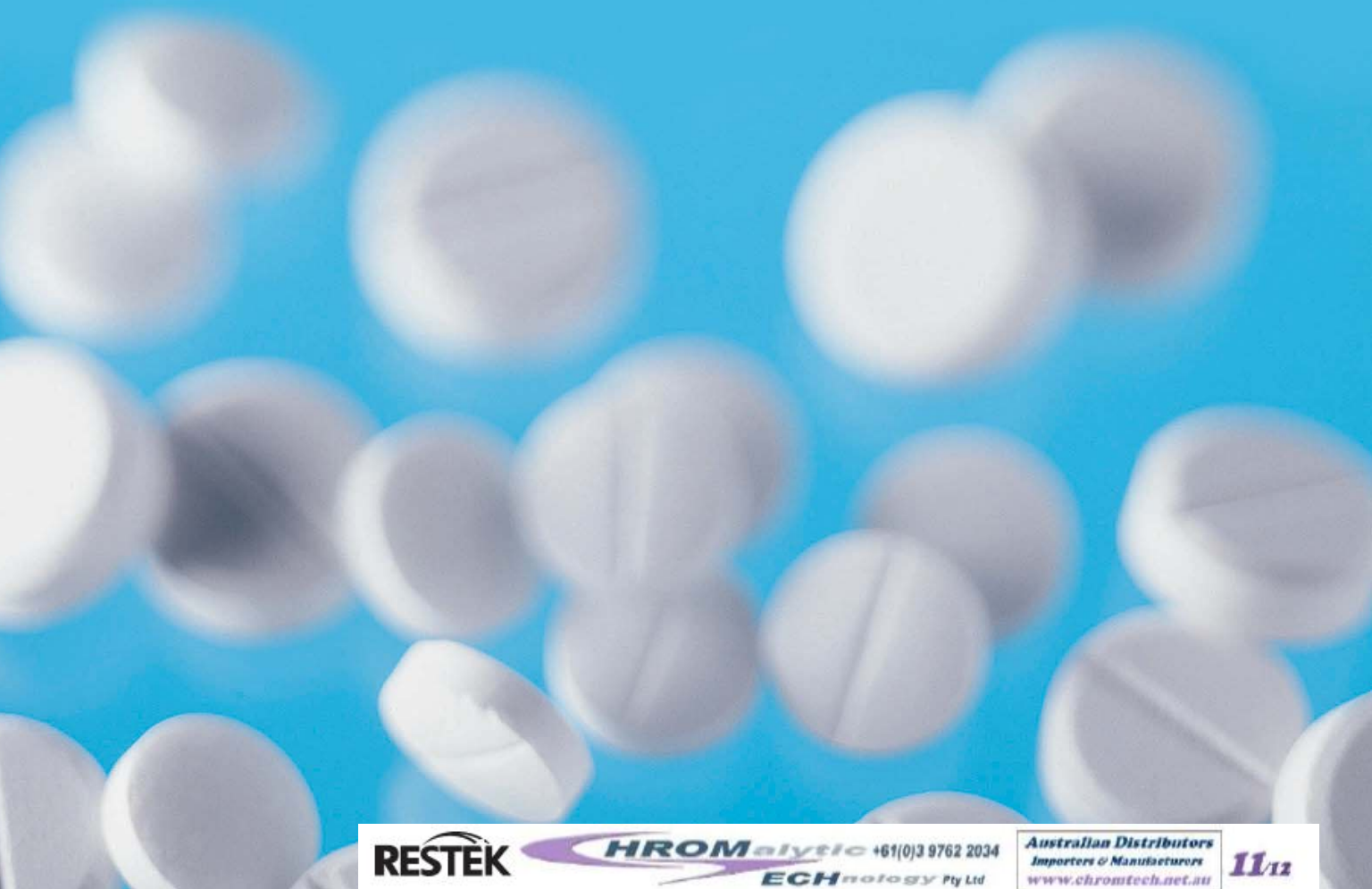
REFERENCE STANDARDS
PHARMACEUTICAL MATERIALS

What's **NEW?** look for this circle



USP <467>

The United States Pharmacopeia (USP) general chapter <467> Residual Solvents is a widely used compendial method intended for identifying and quantifying residual solvents in drug substances, drug products, and excipients. In an attempt to better mirror the International Conference on Harmonization (ICH) guidelines, the USP has adopted a more comprehensive methodology in residual solvent testing—the current USP30/NF25. The ICH publishes a guideline (Q3C) listing the acceptable amounts of solvent residues that can be present. In the ICH guideline, residual solvents are summarized by class, according to their toxicity. Class 1 compounds are carcinogenic compounds that pose a risk to both the consumer and the environment. The use of these solvents is to be avoided, but if they are used, they must be tightly controlled. Class 2 compounds are nongenotoxic animal carcinogens, and concentrations of these compounds should be limited. Chromatographic analysis is needed for both the Class 1 and Class 2 residual solvents.

USP <467> Singles

Volume is 1mL/ampul.

Compound	Solvent	Conc.	cat.# (ea.)	price
acetonitrile	DMSO	2.05mg/mL	36281	
benzene	DMSO	10mg/mL	36282	
carbon tetrachloride	DMSO	20mg/mL	36283	
chlorobenzene	DMSO	1.8mg/mL	36284	
chloroform	DMSO	0.3mg/mL	36285	
cyclohexane	DMSO	19.4mg/mL	36286	
1,1-dichloroethene	DMSO	40mg/mL	36287	
1,2-dichloroethane	DMSO	25mg/mL	36288	
cis-1,2-dichloroethylene	DMSO	4.67mg/mL	36289	
trans-1,2-dichloroethylene	DMSO	4.67mg/mL	36290	
1,2-dimethoxyethane	DMSO	0.5mg/mL	36291	
N,N-dimethylacetamide	DMSO	5.45mg/mL	36292	
N,N-dimethylformamide	DMSO	4.4mg/mL	36293	
1,4-dioxane	DMSO	1.9mg/mL	36294	
2-ethoxyethanol	DMSO	0.8mg/mL	36295	
ethylbenzene	DMSO	1.84mg/mL	36296	
ethylene glycol	DMSO	3.1mg/mL	36297	
formamide	DMSO	1.1mg/mL	36298	
hexane	DMSO	1.45mg/mL	36299	
methanol	DMSO	15mg/mL	36401	
2-methoxyethanol	DMSO	0.25mg/mL	36402	
methylbutylketone	DMSO	0.25mg/mL	36400	
methylcyclohexane	DMSO	5.9mg/mL	36403	
methylene chloride (dichloromethane)	DMSO	3mg/mL	36404	
N-methylpyrrolidone	DMSO	2.65mg/mL	36405	
nitromethane	DMSO	0.25mg/mL	36406	
pyridine	DMSO	1mg/mL	36407	
sulfolane	DMSO	0.8mg/mL	36413	
tetrahydrofuran (THF)	DMSO	3.6mg/mL	36408	
tetralin	DMSO	0.5mg/mL	36409	
toluene	DMSO	4.45mg/mL	36410	
1,1,1-trichloroethane	DMSO	50mg/mL	36411	
trichloroethene	DMSO	0.4mg/mL	36412	
m-xylene	DMSO	6.51mg/mL	36414	
o-xylene	DMSO	0.97mg/mL	36415	
p-xylene	DMSO	1.52mg/mL	36416	

DMSO = dimethyl sulfoxide

These mixtures reflect the changes made in USP30/NF25 effective July 1, 2008.

Residual Solvents - Class 1 (5 components)

benzene	10mg/mL	1,1-dichloroethene	40
carbon tetrachloride	20	1,1,1-trichloroethane	50
1,2-dichloroethane	25		

In dimethyl sulfoxide, 1mL/ampul

cat. # 36279 (ea.)

Residual Solvents Class 2 - Mix A (15 components)

acetonitrile	2.05mg/mL	methylcyclohexane	5.90
chlorobenzene	1.80	methylene chloride	3.00
cyclohexane	19.40	tetrahydrofuran	3.45
cis-1,2-dichloroethene	4.70	toluene	4.45
trans-1,2-dichloroethene	4.70	*m*-xylene	6.51
1,4-dioxane	1.90	*o*-xylene	0.98
ethylbenzene	1.84	*p*-xylene	1.52
methanol	15.00		

In dimethyl sulfoxide, 1mL/ampul

cat. # 36271 (ea.)

Residual Solvents Class 2 - Mix B (8 components)

chloroform	60µg/mL	nitromethane	50
1,2-dimethoxyethane	100	pyridine	200
n-hexane (C6)	290	tetralin	100
2-hexanone	50	trichloroethene	80

In dimethyl sulfoxide, 1mL/ampul

cat. # 36280 (ea.)

Residual Solvents Class 2 - Mix C (8 components)

2-ethoxyethanol	800µg/mL	2-methoxyethanol (methyl Cellosolve)	250
ethylene glycol	3,100	N-methylpyrrolidone	2,650
formamide	1,100	sulfolane	800
N,N-dimethylacetamide	5,450		
N,N-dimethylformamide	4,400		

In dimethyl sulfoxide, 1mL/ampul

cat. # 36273 (ea.)

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OVI retention index

For a list of OVI retention times, see **pages 693 and 696**.

USP <467> *cont'd*

These Class 1 mixtures reflect the changes made in USP24/NF19 effective January 1, 2000, and USP23/NF18 effective January 1, 1995 to December 31, 1999. While these mixtures do not meet the current USP guidelines, many labs still use these mixtures to obtain a detectable benzene peak for the direct injection methods, Method I and Method V.

USP <467> Calibration Mix #7 (4 components)

chloroform	60µg/mL	methylene chloride	600
1,4-dioxane	380	trichloroethene	80

In dimethyl sulfoxide, 1mL/ampul
cat. # 36009 (ea.)

USP <467> Calibration Mix #6 (4 components)

chloroform	60µg/mL	methylene chloride	600
1,4-dioxane	380	trichloroethene	80

In methanol, 1mL/ampul
cat. # 36008 (ea.)

USP <467> Calibration Mixture #5 (5 components)

benzene	2µg/mL	methylene chloride	600
chloroform	60	trichloroethene	80
1,4-dioxane	380		

In dimethyl sulfoxide, 1mL/ampul
cat. # 36007 (ea.)

USP <467> Calibration Mixture #4 (5 components)

benzene	2µg/mL	methylene chloride	600
chloroform	60	trichloroethene	80
1,4-dioxane	380		

In methanol, 1mL/ampul
cat. # 36006 (ea.)

USP <467> Calibration Mixture #2 (5 components)

benzene	100µg/mL	methylene chloride	500
chloroform	50	trichloroethene	100
1,4-dioxane	100		

In methanol, 1mL/ampul
cat. # 36002 (ea.)

USP <467> Calibration Mixture #3 (5 components)

benzene	100µg/mL	methylene chloride	500
chloroform	50	trichloroethene	100
1,4-dioxane	100		

In dimethyl sulfoxide, 1mL/ampul
cat. # 36004 (ea.)

Ethylene Oxide

500µg/mL in dimethyl sulfoxide, 1mL/ampul
cat. # 36005 (ea.)

Ethylene oxide is available in other solvents and concentrations. Request your custom formulation at standards@restek.com.

Limit of Diethylene & Ethylene Glycol Standards

Meet new FDA *Guidance for Industry: Testing of Glycerin for Diethylene Glycol* with our new diethylene glycol (DEG) and ethylene glycol limit standards. This Guidance emphasizes the importance of screening raw material for the presence of diethylene glycol. Under cGMPs, drug manufacturers—not just glycerin manufacturers—must now test glycerin prior to use to prevent DEG-contamination in finished products. FDA has worked extensively with USP to modify the glycerin monograph and these standards support the revised USP method.

Glycerin Standard Mix (3 components)

diethylene glycol	0.5mg/mL	glycerin	20
ethylene glycol	0.5		

In P&T methanol, 1mL/ampul
cat. # 31891 (ea.)

Propylene Glycol Standard Mix (3 components)

diethylene glycol	0.5mg/mL	propylene glycol	20
ethylene glycol	0.5		

In P&T methanol, 1mL/ampul
cat. # 31892 (ea.)

Sorbitol Standard Mix (2 components)

diethylene glycol ethylene glycol
0.8mg/mL each in acetone:water (90:10), 1mL/ampul
cat. # 31893 (ea.)

Limit of Diethylene & Ethylene Glycol Internal Standard Mix

2,2,2-trichloroethanol
10mg/mL in P&T methanol, 1mL/ampul
cat. # 31894 (ea.)

European Pharmacopoeia Method

The analysis of residual solvents in pharmaceutical products has changed, particularly for products being sold into Europe. The International Conference on Harmonization (ICH) *Guidelines for Residual Solvents* is becoming the international standard and is being adopted by more pharmacopoeias, including the United States Pharmacopeia, every year. The ICH method and compound list is more extensive than any method previously used and poses new challenges. Compounds in Class 1 are solvents considered to be of highest risk and to be avoided in pharmaceutical manufacturing. Use of Class 2 compounds is to be limited, as they pose a lower, but present, threat to health. Compounds in Class 3 pose the lowest toxic potential and may be used routinely in manufacturing.

European Pharmacopoeia/ICH Class 1 Mix (5 components)

benzene	2µg/mL	1,1-dichloroethene	8
carbon tetrachloride	4	1,1,1-trichloroethane	1500
1,2-dichloroethane	5		

Prepared in water:dimethyl sulfoxide (90:10), 1mL/ampul
cat. # 36228 (ea.)

European Pharmacopoeia/ICH Class 1 Mix (revised)

(5 components)

benzene	2µg/mL	1,1-dichloroethene	8
carbon tetrachloride	4	1,1,1-trichloroethane	10
1,2-dichloroethane	5		

In water:dimethyl sulfoxide (90:10), 1mL/ampul
cat. # 36261 (ea.)

European Pharmacopoeia Method *cont'd*

European Pharmacopoeia/ICH Q3C(M) Class 2 Mix C, Revised

(6 components)

2-ethoxyethanol	160µg/mL	N-methylpyrrolidone	530
ethylene glycol	620	sulfolane	160
formamide	220		
2-methoxyethanol (methyl Cellosolve)	50		

In dimethyl sulfoxide, 1mL/ampul

cat. # 36275 (ea.)

European Pharmacopoeia/ICH Class 2 Mix B, Revised

NEW!

(10 components)

acetonitrile	410µg/mL	2-hexanone	50
chloroform	60	methanol	3,000
1,2-dimethoxyethane	100	nitromethane	50
N,N-dimethylacetamide	1,090	pyridine	200
1,4-dioxane	380	tetralin	100

Prepared in water:dimethyl sulfoxide (80:20), 1mL/ampul

cat. # 36270 (ea.)

European Pharmacopoeia/ICH Q3C(M) Class 2 Mix A, Revised

(14 components)

chlorobenzene	360µg/mL	methylene chloride	600
cyclohexane	3,880	tetrahydrofuran	720
cis-1,2-dichloroethene	1,870	toluene	890
N,N-dimethylformamide	880	trichloroethene	80
ethylbenzene	369	*m*-xylene	1,302
n-hexane (C6)	290	*o*-xylene	195
methylcyclohexane	1,180	*p*-xylene	304

In dimethyl sulfoxide, 1mL/ampul

cat. # 36274 (ea.)

Composition of Fatty Acids by GC

EP 2.4.22 Composition of Fatty Acids by GC Mix 1

(6 components)

Description	% by Weight	Description	% by Weight
methyl arachidate (C20:0)	40	methyl oleate (C18:1[*cis*9])	20
methyl dodecanoate (C12:0)	5	methyl palmitate (C16:0)	10
methyl myristate (C14:0)	5	methyl stearate (C18:0)	20

100mg total

cat. # 35100 (ea.)

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No data pack available.

Quantity discounts not available.

EP 2.4.22 Composition of Fatty Acids by GC Mix 2

(5 components)

Description	% by Weight	Description	% by Weight
methyl caproate (C6:0)	10	methyl dodecanoate (C12:0)	20
methyl caprylate (C8:0)	10	methyl myristate (C14:0)	40
methyl decanoate (C10:0)	20		

100mg total

cat. # 35101 (ea.)

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ASTM Method D6042-96 (Plastic Container Testing)

American Society for Testing and Materials (ASTM International) Method D6042-96—*Test Method for Determination of Phenolic Antioxidants and Erucamide Slip Additives in Polypropylene Homopolymer Formulations Using Liquid Chromatography*—is a "consensus" or "referee" method used among plastic manufacturers and the pharmaceutical companies that purchase plastic containers. Plastic container manufacturers use this test to ensure the quality of their product to their pharmaceutical customers. Pharmaceutical companies also specify this test and provide their own lists of target compounds and concentration limits in purchase agreements.

This test calls for isopropanol extraction, HPLC separation, and UV detection. Restek offers a variety of reversed phase HPLC columns suitable for these separations. Restek also designed an analytical reference material to validate this method. This mixture contains the common antioxidants and slips listed in ASTM D6042-96, along with BHT.

ASTM D6042-96 Calibration Mix (7 components)

BHT	Irganox 3114
erucamide slip	Irganox 1010
vitamin E	Irganox 1076
Irgafos 168	

50µg/mL each in isopropanol, 1mL/ampul

cat. # 31628 (ea.)

No data pack available.

ASTM D6042-96 Internal Standard Mix

Tinuvin P

51.8µg/mL in isopropanol, 1mL/ampul

cat. # 31629 (ea.)

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Other Additives—Available from Restek as Custom Formulations

Similar methods for extractables in plastic pharmaceutical containers are cited in the United States Pharmacopeia (USP), British Pharmacopeia (BP), European Pharmacopoeia (EP), and Japanese Pharmacopoeia (JP). Customers may also have formulation-specific or product-specific test mixtures. Please contact us for a custom mixture. Our current inventory of raw materials includes these popular antioxidants. We have many more not listed and can obtain most compounds you may need.

- Ethanox 323
- Ethanox 330
- Ethanox 702
- Ethanox 703
- Irganox L06
- Irganox L57
- Irganox L64
- Irganox L109
- Irganox L134
- Irganox L135
- Irganox 1035
- Santanox R
- Ultranox 626
- Vanlube 81
- Vanlube 848
- Vanlube 7723
- Vanlube AZ
- Vanlube NA
- Vanlube PCX
- Vanlube SL
- Vanlube SS