

Pharmaceuticals

Analytical Standards for USP <232>, <233>, <467>, and ICH/Global Compliance

SPEX CertiPrep's comprehensive experience in creating quality pharmaceutical standards will help you to comply with the guidelines set by the United States Pharmacopeia (USP) and the International Conference on Harmonization (ICH) to provide accurate, quantifiable results for the metal analysis in drugs, pharmaceutical substances and raw materials.

For additional product information, please visit www.spexcertiprep.com/products/USP.

USP <232> and USP<233> Elemental Impurities

USP <232> outlines new limits and USP <233> outlines procedures in pharmaceutical products for arsenic, cadmium, lead, and mercury. The proposed procedures focus on the use of ICP-MS (Inductively Coupled Plasma-Mass Spectrometry) for the analysis of low level impurities.

SPEX CertiPrep is proud to offer Elemental Impurities Certified Reference Materials designed for use in USP <232> and USP <233>. These standards can be used as a calibration or check standard to verify Oral Daily Dose PDE, Parenteral Component Limit or Parenteral Daily Dose PDE.

Oral Elemental Impurities A

Element	Concentration	Volume	Matrix	Part #
Arsenic	15 mg/kg	125 mL	5% HNO ₃ /1% HCl	USP-TXM2A
Cadmium	5 mg/kg			
Lead	5 mg/kg			
Mercury	30 mg/kg			

Precious Metal Impurities B (with Os)

Element	Concentration	Volume	Matrix	Part #
Iridium	100 mg/kg for each component	125 mL	15% HCl	USP-TXM3
Osmium				
Palladium				
Platinum				
Rhodium				
Ruthenium				

CERTIFIED REFERENCE MATERIALS

Since 1954, SPEX CertiPrep is the industry leader in the CRM marketplace meeting the needs of laboratories worldwide with innovation and research. Accredited by A2LA to ISO/IEC 17025:2017 & ISO 17034:2016. Certified by DQS to ISO 9001:2015.

Pharmaceuticals (cont'd)

Precious Metal Impurities B (without Os)				
Element	Concentration	Volume	Matrix	Part #
Iridium	100 mg/kg for each component	125 mL	15% HCl	USP-TXM4
Palladium				
Platinum				
Rhodium				
Ruthenium				

Oral Elemental Impurities C				
Element	Concentration	Volume	Matrix	Part #
Chromium	11,000 mg/kg	125 mL	5% HNO ₃	USP-TXM5A
Copper	3,000 mg/kg			
Molybdenum	3,000 mg/kg			
Nickel	200 mg/kg			
Vanadium	100 mg/kg			

Parenteral Elemental Impurities C				
Element	Concentration	Volume	Matrix	Part #
Chromium	1,100 mg/kg	125 mL	5% HNO ₃	USP-TXM5B
Copper	300 mg/kg			
Molybdenum	1,500 mg/kg			
Nickel	20 mg/kg			
Vanadium	10 mg/kg			

Parenteral Elemental Impurities D				
Element	Concentration	Volume	Matrix	Part #
Arsenic	15 mg/kg	125 mL	5% HNO ₃ /1% HCl	USP-TXM6A
Cadmium	2 mg/kg			
Lead	5 mg/kg			
Mercury	3 mg/kg			

USP <467> Residual Solvents

The USP General Chapter <467> Residual Solvents is a method widely used for identifying and quantifying residual solvents when there is no information available on what solvents are likely to be present.

SPEX CertiPrep now offers 35 analytes in dimethyl sulfoxide for Class 1, Class 2 and Class 3 solvents. Our products are manufactured and verified by our QC department to validate the Certificate of Analysis which accompanies each product.

5 Organic Volatile Impurities: Class 1 Solvents					
Compound	CAS #	Concentration	Volume	Matrix	Part #
Benzene	71-43-2	10,000 µg/mL	1 mL	Dimethyl Sulfoxide	USP-RS-C1
Carbon tetrachloride	56-23-5	20,000 µg/mL			
1,2-Dichloroethane	107-06-2	25,000 µg/mL			
1,1-Dichloroethene	75-35-4	40,000 µg/mL			
1,1,1-Trichloroethane	71-55-6	50,000 µg/mL			

15 Organic Volatile Impurities: Class 2 Solvents

Compound	CAS #	Concentration	Volume	Matrix	Part #
Acetonitrile	75-05-8	2,050 µg/mL	1 mL	Dimethyl Sulfoxide	USP-RS-C2A
Chlorobenzene	108-90-7	1,800 µg/mL			
Cyclohexane	110-82-7	19,400 µg/mL			
cis-1,2-Dichloroethene	156-59-2	4,700 µg/mL			
trans-1,2-Dichloroethene	156-60-5	4,700 µg/mL			
1,4-Dioxane	123-91-1	1,900 µg/mL			
Ethylbenzene	100-41-4	1,840 µg/mL			
Methanol	67-56-1	15,000 µg/mL			
Methylcyclohexane	108-87-2	5,900 µg/mL			
Methylene chloride	75-09-2	3,000 µg/mL			
Tetrahydrofuran	109-99-9	3,450 µg/mL			
Toluene	108-88-3	4,450 µg/mL			
m-Xylene	108-38-3	6,510 µg/mL			
o-Xylene	95-47-6	980 µg/mL			
p-Xylene	106-42-3	1,520 µg/mL			

8 Organic Volatile Impurities: Class 2 Solvents

Compound	CAS #	Concentration	Volume	Matrix	Part #
Chloroform	67-66-3	60 µg/mL	1 mL	Dimethyl Sulfoxide	USP-RS-C2B
1,2-Dimethoxyethane	110-71-4	100 µg/mL			
n-Hexane	110-54-3	290 µg/mL			
2-Hexanone	597-78-6	50 µg/mL			
Nitromethane	75-52-5	50 µg/mL			
Pyridine	110-86-1	200 µg/mL			
1,2,3,4-Tetrahydronaphthalene	119-64-2	100 µg/mL			
Trichloroethene	79-01-6	80 µg/mL			

8 Organic Volatile Impurities: Class 2 Solvents

Compound	CAS #	Concentration	Volume	Matrix	Part #
N,N-Dimethylacetamide	127-19-5	5,450 µg/mL	1 mL	Dimethyl Sulfoxide	USP-RS-C2C
N,N-Dimethylformamide	68-12-2	4,400 µg/mL			
2-Ethoxyethanol	110-80-5	800 µg/mL			
Ethylene glycol	107-21-1	3,100 µg/mL			
Formamide	75-12-7	1,100 µg/mL			
2-Methoxyethanol	109-86-4	250 µg/mL			
1-Methyl-2-pyrrolidinone	872-50-4	2,650 µg/mL			
Tetramethylene sulfone	126-33-0	800 µg/mL			

2 Organic Volatile Impurities: Class 3 Solvents

Compound	CAS #	Concentration	Volume	Matrix	Part #
Acetic acid	67-19-7	1,000 µg/mL for each component	1 mL	Dimethyl Sulfoxide	USP-RS-C3B
Formic acid	64-18-6				

24 Organic Volatile Impurities: Class 3 Solvents

Compound	CAS #	Concentration	Volume	Matrix	Part #
Acetone	67-64-1	1,000 µg/mL for each component	1 mL	Dimethyl Sulfoxide	USP-RS-C3A
Anisole	100-66-3				
2-Butanone	78-93-3				
1-Butanol	71-36-3				
2-Butanol	78-92-2				
Butyl acetate	123-86-4				
tert-Butyl methyl ether	1634-04-4				
Ethanol	64-17-5				
Ether	60-29-7				
Ethyl acetate	141-78-6				
Ethyl formate	109-94-4				
n-Heptane	142-82-5				
Isobutyl acetate	110-19-0				
Isopropyl acetate	108-21-4				
Isopropyl benzene	98-82-8				
Methyl acetate	79-20-9				
3-Methyl-1-butanol	123-51-3				
4-Methyl-2-pentanone	108-10-1				
2-Methyl-1-propanol	78-83-1				
n-Pentane	109-66-0				
1-Pentanol	71-41-0				
1-Propanol	71-23-8				
2-Propanol (Isopropanol, Isopropyl alcohol)	67-63-0				
Propyl acetate	109-60-4				

USP <467> Residual Solvent Singles

Compound	CAS #	Concentration	Volume	Matrix	Part #
Acetonitrile	75-05-8	2,050 µg/mL	1 mL	Dimethyl sulfoxide	USP-S145-DMSO
Benzene	71-43-2	10,000 µg/mL	1 mL	Dimethyl sulfoxide	USP-S405-DMSO
Carbon tetrachloride	56-23-5	20,000 µg/mL	1 mL	Dimethyl sulfoxide	USP-S750-DMSO
Chlorobenzene	108-90-7	1,800 µg/mL	1 mL	Dimethyl sulfoxide	USP-S810-DMSO
Chloroform	67-66-3	300 µg/mL	1 mL	Dimethyl sulfoxide	USP-S865-DMSO
Cyclohexane	110-82-7	19,400 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1015-DMSO
1,2-Dichloroethane	107-06-2	25,000 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1380-DMSO
1,1-Dichloroethene	75-35-4	40,000 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1390-DMSO
cis-1,2-Dichloroethene	156-59-2	4,670 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1394-DMSO
trans-1,2-Dichloroethene	156-60-5	4,670 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1400-DMSO
1,2-Dimethoxyethane	110-71-4	500 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1572-DMSO
N,N-Dimethylacetamide	127-19-5	5,450 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1597-DMSO
N,N-Dimethylformamide	68-12-2	4,400 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3897-DMSO
1,4-Dioxane	123-91-1	1,900 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1715-DMSO
2-Ethoxyethanol	110-80-5	800 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1910-DMSO
Ethylbenzene	100-41-4	1,840 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1940-DMSO
Ethylene glycol	107-21-1	3,100 µg/mL	1 mL	Dimethyl sulfoxide	USP-S1952-DMSO
Formamide	75-12-7	1,100 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2062-DMSO
n-Hexane	110-54-3	1,450 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2190-DMSO
2-Hexanone	591-78-6	250 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2200-DMSO
Methanol	67-56-1	15,000 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2380-DMSO
2-Methoxyethanol	109-86-4	250 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2407-DMSO
Methylcyclohexane	108-87-2	5,900 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2470-DMSO
Methylene chloride	75-09-2	3,000 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2480-DMSO
1-Methyl-2-pyrrolidinone	872-50-4	2,650 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2590-DMSO
Nitromethane	75-52-5	250 µg/mL	1 mL	Dimethyl sulfoxide	USP-S2722-DMSO

USP <467> Residual Solvent Singles (cont'd)

Compound	CAS #	Concentration	Volume	Matrix	Part #
Pyridine	110-86-1	1,000 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3240-DMSO
Tetrahydrofuran	109-99-9	3,600 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3460-DMSO
1,2,3,4-Tetrahydronaphthalene	119-64-2	500 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3464-DMSO
Tetramethylene sulfone	126-33-0	800 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3877-DMSO
Toluene	108-88-3	4,450 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3505-DMSO
1,1,1-Trichloroethane	71-55-6	50,000 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3605-DMSO
Trichloroethene	79-01-6	400 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3615-DMSO
m-Xylene	108-38-3	6,510 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3830-DMSO
o-Xylene	95-47-6	970 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3835-DMSO
p-Xylene	106-42-3	1,520 µg/mL	1 mL	Dimethyl sulfoxide	USP-S3840-DMSO

ICH/Global Compliance Standards

The International Conference for Harmonization (ICH) has produced a concept paper proposing a new guideline intended to provide a global policy for qualitatively and quantitatively limiting metal impurities in drug ingredients and finished products. The new proposed guideline (Q3D) would provide clarification of the requirements for metals, which are included in the ICH inorganic impurities classification.

SPEX CertiPrep is proud to offer a line of analytical standards for the analysis of trace metals in pharmaceutical materials. These standards can be used as a calibration or check standard to verify all component or dosage limits.

Oral Elemental Impurities A

Element	Concentration	Volume	Matrix	Part #
Arsenic	1.5 mg/kg	125 mL	5% HNO ₃	ICH-TXM2
Cadmium	25 mg/kg			
Lead	5 mg/kg			
Mercury	15 mg/kg			

Precious Metal Impurities B (with Os)

Element	Concentration	Volume	Matrix	Part #
Iridium	100 mg/kg for each component	125 mL	15% HCl	ICH-TXM3
Osmium				
Palladium				
Platinum				
Rhodium				
Ruthenium				

Precious Metal Impurities B (without Os)

Element	Concentration	Volume	Matrix	Part #
Iridium	100 mg/kg for each component	125 mL	15% HCl	ICH-TXM4
Palladium				
Platinum				
Rhodium				
Ruthenium				

Elemental Impurities E				
Element	Concentration	Volume	Matrix	Part #
Chromium	250 mg/kg	125 mL	5% HNO ₃	ICH-TXM7
Cobalt	100 mg/kg			
Copper	1,000 mg/kg			
Manganese	2,500 mg/kg			
Molybdenum	100 mg/kg			
Nickel	250 mg/kg			
Vanadium	100 mg/kg			

Elemental Impurities F				
Element	Concentration	Volume	Matrix	Part #
Iron	13,000 mg/kg for each component	125 mL	5% HNO ₃	ICH-TXM8
Zinc				

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US ADDRESS

203 Norcross Avenue • Metuchen, NJ 08840
 Tel: 1.800.LAB.SPEX • +1.732.549.7144 • Fax: 732.603.9647
 CRMSales@spex.com • www.spexcertiprep.com

UK ADDRESS

2 Dalston Gardens • Stanmore, Middlesex • HA7 1BQ • UK
 Tel: +44 (0) 208 204 6656 • Fax: +44 (0) 208 204 6654
 SPEXEurope@spex.com • www.SPEXEurope.com