#### SCAVENGER RESINS FOR REMOVING METAL SPECIES



Organometallic compounds are commonly used in drug discovery as metal reagents or metal catalysts. However, many of these compounds remain associated with the target compound and may present a risk to health. Guidelines limit exposure to metals suspected of significant toxicity.

The StratoSpheres range includes a number of products that reduce residual metal content to permissible levels.

#### **Key Benefits**

- ▶ Rapid and convenient. Compatible with high throughput technologies and simple manual operation.
- Macroporous, open structure. Allows rapid diffusion across the broadest range of solvents.
- Wide choice of functionality. Suitable for removal of many different metal species.
- **Cost effective.** Economical and simple to use, requiring no specialized laboratory equipment or instrumentation.
- Optimized spherical particle size. For easy handling and rapid filtration.
- Available as pre-packed cartidges and bulk media.

  Covering a wide range of synthesis scales, from R&D upwards.

NOTICE: This document contains references to Varian. Please note that Varian, Inc. is now part of Agilent Technologies. For more information, go to www.agilent.com/chem.



#### Organometallics in Drug Discovery

Organometallic compounds are commonly used in the pharmaceutical industry as part of the drug-discovery process. During high-throughput synthesis, organometallics are often employed as catalysts because they facilitate unusual and useful synthetic transformations. Chiral structures, carbon-carbon bonds and other reactions are frequently accomplished using organometallic reagents. However, the properties that make such compounds synthetically useful can also lead to cytotoxic effects. It is, therefore, very important that compounds prepared using organometallic compounds have very low levels of residual metal content.

The European Medicines Agency (EMEA) and US Pharmacopeia (USP) publish guidelines on the maximum concentration limits for a number of different metal species. Many of these limits are <1 ppm.

## Methods of Removal

A number of approaches have been tried to reduce the overall residual metal content of pharmaceutical compounds. In some cases, solvent extraction is sufficient but other commercial remedies may rely on precipitation.

A much more convenient approach is to pass the solution through an SPE device, containing a StratoSpheres metal chelating sorbent. Many functionalities are available and it is a simple matter to screen a selection of sorbents to find which ligand competes most effectively to remove the unwanted metal contaminant.

The StratoSpheres range includes a wide variety of polymeric particles in both microporous (swellable) and macroporous (MP) (non-swellable) forms. They are available in convenient SPE cartridges for small-scale use and in loose media and bulk (multi-kg) quantities for larger requirements. To aid the screening process, StratoSpheres toolkits contain a selection of appropriate sorbents.

#### Metals of Particular Interest

The Periodic Table identifies a number of metals "of significant safety concern", many of which are commonly used in API (active pharmaceutical ingredient) synthesis.



#### Products for Metal Removal

There are a number of ligands/ligand combinations suitable for chelating metal species. However, it is not always possible to anticipate which product works best under a given set of conditions. Reaction temperature, concentration, solvent, and the presence of other species may all influence the outcome, and so we recommend screening a selection of products, including:

#### Sulfur

PL-BnSH	CH₂SH
PL-BnSH MP	
PL-Thiol MP	

#### Ion Exchange

PL-S03H	SO₃H
PL-S03H MP	

#### Sulfur / Nitrogen

PL-Thiourea MP	О Н Н СН₃
PL-TMT MP	SH SH

#### Nitrogen

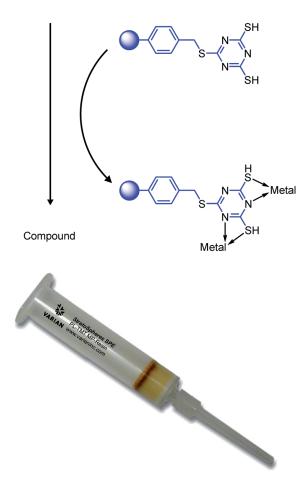
PL-Urea MP	NH H CH₃
PL-TBD PL-TBD MP PL-Guanidine MP	
PL-DETA PL-DETA MP	NH NH₂

#### Illustrative Example

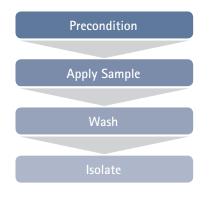
The efficacy of StratoSpheres metal removal products relies on their ability to sequester metals from solution through a strong interaction.

The coordinating effect of nitrogen and sulfur ligands is exploited in these materials, particularly in PL-TMT MP Resin.

#### Compound-----Metal



#### Simple Protocol



**Pre-condition** the sorbent by rinsing with methanol (or similar solvent). This helps to overcome surface tension effects by "wetting" the sorbent.

Apply Sample solution and allow to percolate through under gravity, or stir a suspension containing the sorbent. Collect filtrate containing metal-free product.

Wash sorbent with methanol and collect filtrate.

Isolate compound from combined filtrate and washings.

#### **Ordering Information**

MP indicates macroporous products that are used with the widest range of solvents. All other products are microporous and are suitable for use in "good" organic solvents, which swell the beads.

Description	Pack Size (g)	Part No.	Pack Size (g)	Part No.	Pack Size (g)	Part No.	Pack Size (kg)	Part no.
Palladium Scavenging Toolkit, 6 x 5 g		PL3498-0005	(Comprising PL-BnSH MP, PL-DETA MP, PL-EDA MP, PL-TBD MP, PL-Thiourea MP, PL-TMT MP)				BD MP,	
PL-BnSH Resin 1.8 mmol/g 150-300 μm	5	PL3482-1689	25	PL3482-3689	100	PL3482-4689	1	PL3482-6689
PL-BnSH MP Resin 2.2 mmol/g 100Å 150-300 μm	5	PL3582-1689	25	PL3582-3689	100	PL3582-4689	1	PL3582-6689
PL-DETA Resin >6.0 mmol N/g 150-300 μm	5	PL3401-1679	25	PL3401-3679	100	PL3401-4679	1	PL3401-6679
PL-DETA MP Resin >4.5 mmol N/g 100Å 150-300 μm	5	PL3501-1679	25	PL3501-3679	100	PL3501-4679	1	PL3501-6679
PL-S03H Resin >3.5 mmol/g 150-300 μm	5	PL3404-1679	25	PL3404-3679	100	PL3404-4679	1	PL3404-6679
PL-SO3H MP Resin >3.0 mmol/g 100Å 150-300 μm	5	PL3504-1679	25	PL3504-3679	100	PL3504-4679	1	PL3504-6679
PL-TBD Resin 2.7 mmol/g 150-300 μm	5	PL3414-1679	25	PL3414-3679	100	PL3414-4679	1	PL3414-6679
PL-TBD MP Resin 1.7 mmol/g 100Å 150-300 μm	5	PL3514-1679	25	PL3514-3679	100	PL3514-4679	1	PL3514-6679
PL-Thiourea MP Resin >2.0 mmol/g 100Å 150-300 μm	5	PL350B-1689	25	PL350B-3689	100	PL350B-4689	1	PL350B-6689
PL-TMT MP Resin >0.6 mmol/g 100Å 150-300 μm	5	PL3527-1679	25	PL3527-3679	100	PL3527-4679	1	PL3527-6679
PL-Urea MP Resin >2.0 mmol/g 100Å 150-300 μm	5	PL350A-1689	25	PL350A-3689	100	PL350A-4689	1	PL350A-6689

Description	Pack Quantity	Part No.	
Metal Removal SPE Screening Kit (500 mg/6 mL)	50	PL3540-0099	(Comprising PL-Guanidine MP SPE, PL-Thiol MP SPE, PL-Thiourea MP SPE, PL-TMT MP SPE, PL-Urea MP SPE)
PL-Guanidine MP SPE (500 mg/6 mL)	50	PL3514-CM89	
PL-SO3H MP SPE (500 mg/6 mL)	50	PL3504-C679	
PL-Thiol MP SPE (500 mg/6 mL)	50	PL3582-CM89	
PL-Thiourea MP SPE (500 mg/6 mL)	50	PL350A-CM89	
PL-TMT MP SPE (500 mg/6 mL)	50	PL3527-CM89	
PL-Urea MP SPE (500 mg/6 mL)	50	PL350B-CM89	

#### Accessories

These allow larger volumes of solution to pass through the pre-packed cartridges.

Description	Pack Quantity	Part No.
Adapter caps for 6 mL cartridges	15	12131001
Luer stopcocks	15	12131005
Empty 20 mL reservoir	100	12131011
Empty 60 mL reservoir	100	12131012



Varian, Inc. www.varianinc.com

North America: 800.926.3000, 925.939.2400 Europe The Netherlands: 31.118.67.1000 Asia Pacific Australia: 613.9560.7133 Latin America Brazil: 55.11.3238.0400

Other sales offices and dealers throughout the world–check our Web site.