



User Guide

QuadraPure™ Metal Scavengers



User Guide - QuadraPure™ Metal Scavengers

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User Guide - QuadraPure™ Metal Scavengers

Introduction

The QuadraPure™ range of metal scavengers offers an attractive solution to metal contamination problems associated with pharmaceutical and fine chemical processing. Advantageously, the very low levels of extractable impurities make QuadraPure™ products particularly suitable for GMP-compliant applications in both batch and continuous processing. Regulatory Support Files are available for each of the macroporous QuadraPure™ products to support their use in GMP-standard applications.

Reaxa is pleased to offer alternative purity grades as required for use in process applications where recovery of metal value or bulk waste stream decontamination is the objective. In addition, through partnership with Umicore (www.umicore.com), complete metal management solutions are available.

The QuadraPure™ series can be used in loose resin bead format at R&D through to large-scale bulk process applications. Following recent developments, Reaxa is now positioned to offer the macroporous QuadraPure™ range in pre-packed cartridge format for R&D use plus large-scale (>10Kg QuadraPure™) capacity cartridges developed to be compatible with existing filter housings used in manufacturing plants.

A QuadraPure™ resin metal selector guide is given in Appendix.

As Reaxa is continually enhancing its metal scavenging capabilities, the Company can also offer experimental metal-scavenger products to help solve customer problems across the chemical industry sectors. For further information please contact Reaxa at info@reaxa.com.

Product Availability

For R&D quantities, the QuadraPure™ range is available from Sigma Aldrich (www.sigmaaldrich.com).

For bulk pricing, specific problems and technical assistance please contact Reaxa directly at info@reaxa.com



QuadraPure™ Macroporous Range

<u>Product</u>	<u>Structure</u>	<u>Functional Group</u>
QuadraPure™ TU		Thiourea
QuadraPure™ IDA		Imino Diacetate
QuadraPure™ AMPA		Aminomethyl phosphonic acid
QuadraPure™ BzA		Benzyl amine
QuadraPure™ EDA		Amine
QuadraPure™ BdZ		Imidazole
QuadraPure™ DET		Thiol

QuadraPure™ Microporous Range

<u>Product</u>	<u>Structure</u>	<u>Functional Group</u>
QuadraPure™ MPA		Mercaptophenyl amino
QuadraPure™ AEA		Aminoethyl amino
QuadraPure™ IMDAZ		Imidazol-1-yl propyl amino



QuadraPure™ Macroporous Range

Features and Appearance

- Compatible with organic, aqueous, protic and aprotic media
- Low swelling characteristics making the resins ideal for use in fixed bed applications

Appearance:

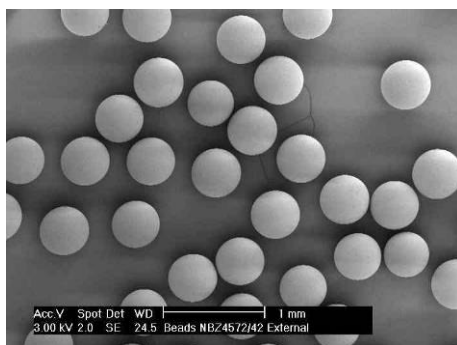


Figure 1 Photograph of QuadraPure™ beads

This macroporous polystyrene QuadraPures™ are highly robust and chemically resistant free-flowing, pale beige beads, 450 – 600 microns in diameter (Fig. 1). The narrow particle size distribution makes these products suitable for use in fixed bed and cartridge format.

Guidelines for Use

Note: For further detailed user application notes and advice on specific problems, please write to info@reaxa.com

Metal-Contaminated Organic Solutions:

In metal contaminated organic solvents, such as DCM, DMF or THF, the QuadraPure™ may be used directly. Typically, add 5g of resin per 100ml of 1000ppm metal-contaminated solution and leave to gently agitate at room temperature for 16-24 hours. Metal removal is often more rapid and is frequently observed by a colour change in both the resin and the starting solution containing the metal contaminant (Fig. 2)*. The resin is simply removed by filtration.

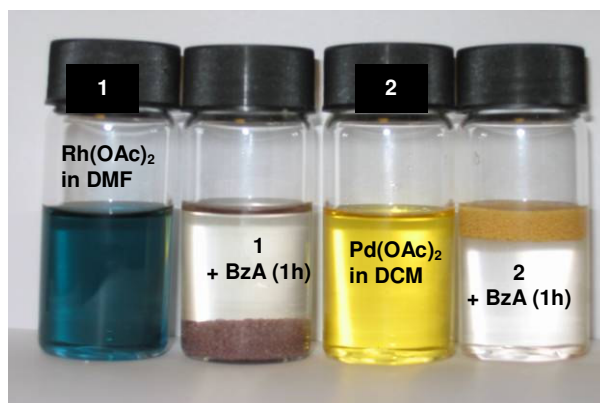


Figure 2 Vials showing the effect of adding QuadraPure™ to solutions containing metal salts



Metal-Contaminated Aqueous Solutions:

If the metal is to be removed from an aqueous system, typically use 5g of resin per 100ml of 1000ppm solution, but in order to aid wetting of the resin the addition of a small amount of a water-miscible organic solvent (such as methanol, ethanol, acetone, etc) may be required. Gently agitate at room temperature for 16-24 hours. Metal removal can often be more rapid than this and is often observed by a colour change in both the resin and the starting solution containing the metal contaminant*. The resin can be simply removed by filtration.

**The rate of metal scavenging can be increased by the addition of more resin, raising the temperature or increasing the agitation rate.*

QuadraPure™ Microporous Range

Features

- High metal capacity
- Fast metal removal

QuadraPure™ MPA, for example, has been successfully used to remove Pd from a solution containing 1200 ppm to obtain a solution of metal to < 1ppm in less than 30 min, using 5g of resin per 100ml solution.

Appearance and Specifications

The microporous QuadraPures™ are glassy, free flowing off-white to pale yellow beads. The beads range in size between 100 - 750 µm in diameter, dependent upon functionality, and they can swell by up to 4x in some organic solvents.

Solvents

The microporous resins can be used in a wide range of mid-polarity organic solvents including DMF, THF, dichloromethane, toluene and ethyl acetate. However, efficiency is reduced in highly polar solvents, for example, methanol, ethanol, water or isopropyl alcohol.

Guidelines for Use

For optimum results swell the resin in THF or DCM for 30 minutes at room temperature prior to use. Then simply add 5g of resin per 100ml of 1000ppm solution and leave to gently agitate at room temperature*. Metal removal can often be observed by a colour change in both the resin and the starting solution containing the metal contaminant (Fig. 2). The resin may be easily removed by filtration.

**Note: the rate of metal scavenging can be improved by the addition of more resin, by raising the temperature or by increasing the agitation rate.*



Quadra Pure™ Applications in Column/Flow Systems

Due to their low swelling characteristics, the macroporous range of QuadraPure™ resins are ideally suited to flow applications, and it has been found indeed that these resins can achieve up to 50% greater metal scavenging capacity when used in flow rather than stirred batch.

The resins can be slurry packed into columns and run with gravity or, ideally for removal of air, a pump can be used to pump the metal containing solution upwards through the column against gravity. Flow rates of between 4 and 10 bed volumes/ hour should be used and these should be sufficient to clean up solutions without the need to recycle over the column. If recycle is necessary the metal remains tightly bound under normal circumstances and does not leach if the solution mixture is recirculated.

Regeneration of the acid functional QuadraPure™ IDA and AMPA can be carried out in column format by flowing an acid regenerant solution through the column at the same flow rates as the metal contaminated solution (ie. 4 to 10 bed volumes /hour). QuadraPure™ TU can be partially recovered by treatment with Na₂S.

Cartridge Applications

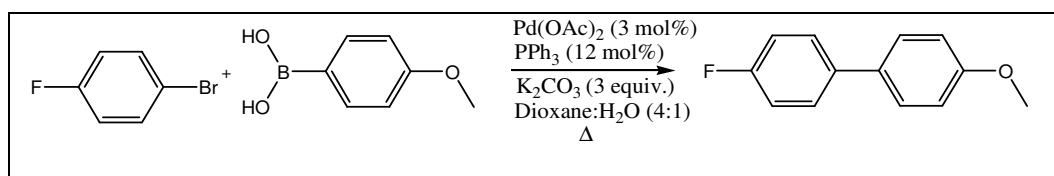
The macroporous range of QuadraPure™ resins can be used in cartridge column format (see Fig. 3).



Figure 3 Cartridge containing QuadraPure™

The following example details how a VersaFlash (www.sigmaaldrich.com) column (Fig. 3) containing QuadraPure™ TU could be used to obtain a 97% reduction in the Pd content following a Suzuki reaction:

Suzuki Reaction





Experimental Procedure

The reaction was performed by adding 4-methoxyphenylboronic acid (13.35g) to 4-bromofluorobenzene (13.35g), palladium acetate (0.52g), triphenylphosphine (2.41g) and potassium carbonate (31.4g) in dioxane:water (450 ml: 50ml). The solution was refluxed for 16h, under N₂. Toluene (200 ml) and water (200 ml) were added and the organic layer separated and washed, using H₂O (2 x 200ml). The resulting organic layer was filtered through Celite to give a yellow solution.

Simple filtration of the solution through a VersaFlash (www.sigmaldrich.com) cartridge packed with QuadraPure™ TU resulted in a 97% reduction in the Pd content.

Further QuadraPure™ Cartridge Applications:

With industry collaborators, the macroporous QuadraPure™ range of products have been successfully packed and used in a variety of cartridges, and encouraging results have been obtained for scavenging metals from organic solutions.

For example, following wetting out of a QuadraPure™ TU cartridge with min 5 column volumes of THF, a solution of 1000ppm of Pd(OAc)₂ in THF is pumped through the cartridge at a flow rate of approximately 4 bed volumes/hr. The system was found to scavenge the Pd from the solution up to the maximum resin capacity. Capacities of 20-25mg Pd/g resin have typically been achieved. IDA and AMPA resin has also been packed into cartridges, and the IDA cartridges have shown scavenging of up to 0.3mmol Cu/g resin. The packed cartridges have shown compatibility with a range of solvents including THF, DCM, DMF, methanol and IPA.

The cartridges are user-friendly and are available in various sizes compatible with standard flash chromatography equipment. Commercial launch of these products is planned for mid 2006. For further details of status of these cartridges please contact info@reaxa.com.

Metal Recovery

For all scavenger resins the value of the metal scavenged may be recuperated by incineration of the resin bound metal. Reaxa is also pleased to offer through partnership with Umicore, (www.umicore.com) complete metal management solutions.

The acid functional IDA and AMPA resins can be liberated and the resins reused many times by treating with acid, for example, 2N HCl.

Resin Regeneration

Regeneration of the acid functional QuadraPure™ IDA and AMPA can be carried out by treatment with aqueous acid (e.g. 2N HCl). QuadraPure TU can be partially recovered by treatment with Na₂S.

Storage

The QuadraPure™ range of products are air-stable and can be stored at room temperature.



APPENDIX

QuadraPure™ Resin Selection Guide

Please note that the following is a guide only and that the efficiency of a metal scavenger will depend upon a number of factors including the oxidation state of the metal involved, pH and potential competing complexation by other ligands present and/ or the solvent. It is normally recommended that a range of QuadraPure™ are assayed for each metal contamination problem.

Metal QP	Ag	Al	Au	Cd	Co	Cu	Fe	Hg	Ni(0)	Ni(II)	Os	Pb	Pd(II)	Pd(0)	Pt	Ru	Rh	Sn	V	Zn
TU	✓✓	-	✓✓	✓✓	✓✓	✓✓	✓	✓✓	✓	✓✓	-	-	✓✓	✓	✓✓	✓✓	✓✓	-	✓	✓✓
IDA	-	✓	-	✓✓	✓✓	✓✓	✓✓	-	✓	✓✓	-	✓✓	✓	✓	-	-	-	-	✓	✓
AMPA	-	✓✓	-	-	✓✓	✓✓	✓✓	-	✓	✓✓	-	-	✓	-	-	-	-	✓	✓✓	✓
IMDAZ	-	-	-	-	✓✓	✓	✓	-	✓✓	✓✓	✓✓	-	✓✓	✓	-	✓✓	✓✓	✓	✓	-
MPA	✓✓	-	✓✓	✓✓	-	✓	-	✓✓	-	✓	-	✓✓	✓✓	✓✓	✓✓	✓✓	-	✓✓	-	-
AEA	-	-	-	-	-	✓	✓	-	-	-	-	-	✓✓	✓	-	-	✓✓	-	✓✓	-
BDZ	-	-	-	-	✓✓	-	-	-	-	✓	-	-	✓✓	-	-	-	✓✓	-	-	-
EDA	-	-	-	-	✓	-	-	-	-	✓✓	-	-	✓✓	✓✓	-	-	✓	-	-	-
BzA	-	-	-	-	✓✓	✓✓	-	-	-	✓✓	-	-	✓✓	-	-	-	✓✓	-	-	-
DET	-	-	-	-	-	✓✓	✓✓	-	-	-	-	-	✓	✓✓	-	-	✓	-	-	-
DTC	-	-	-	-	✓✓	-	✓✓	-	-	✓✓	-	-	✓	✓✓	-	-	✓✓	-	-	-

- ✓✓ Excellent Scavenging Ability (> 99% removal)
- ✓ Significant Scavenging Ability
- Not Tested /No Significant Scavenging Ability