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Heavy Metals Testing via ICP/MS

There have been tremendous changes in the pharmacopeias regarding heavy metals analysis. In December 2014, the final ICH Q3D Guideline came out to harmonize approval requirements under various regulatory regimes. Also, the visual limit value test required under USP <231> is now being replaced by an element-selective and quantitative instrumental measurement technique in accordance with USP <232> and USP <233>. The Ph. Eur. has also recently released new regulations in chapters 5.20 and 2.4.20. Since January 1, 2017, the testing parameters outlined in chapter 2.4.8 (heavy metals) are no longer included in all monographs. Only monograph 0008 (Water purified, Aqua purificata) is excepted from this new regulation. Thus in cases where the current monographs have to be followed, conducting heavy metals analyses is no longer standard procedure.

Due to the large number of analytes and the low determination limits to be achieved, the use of ICP/MS for element determination has vastly gained importance in pharmaceuticals. Eurofins BioPharma Product Testing Hamburg has been a reliable industry partner in this field for many years.

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ICH Q3D Guideline

The final version of the ICH Q3D Guideline (Elemental Impurities) came out in December 2014. Threshold values were established for 24 different elements based on toxicological data for various exposure paths. In a risk assessment of the production process the manufacturer has to identify known and potential sources of impurities and test for these versus the limit values.

The purpose of the Guideline is to harmonize differing regulatory requirements under various regional regulatory regimes. However, there are considerable implementation differences between the USP and EP regulations regarding both the selection of elements and the setting of limit values.

EP 5.20 and 2.4.20

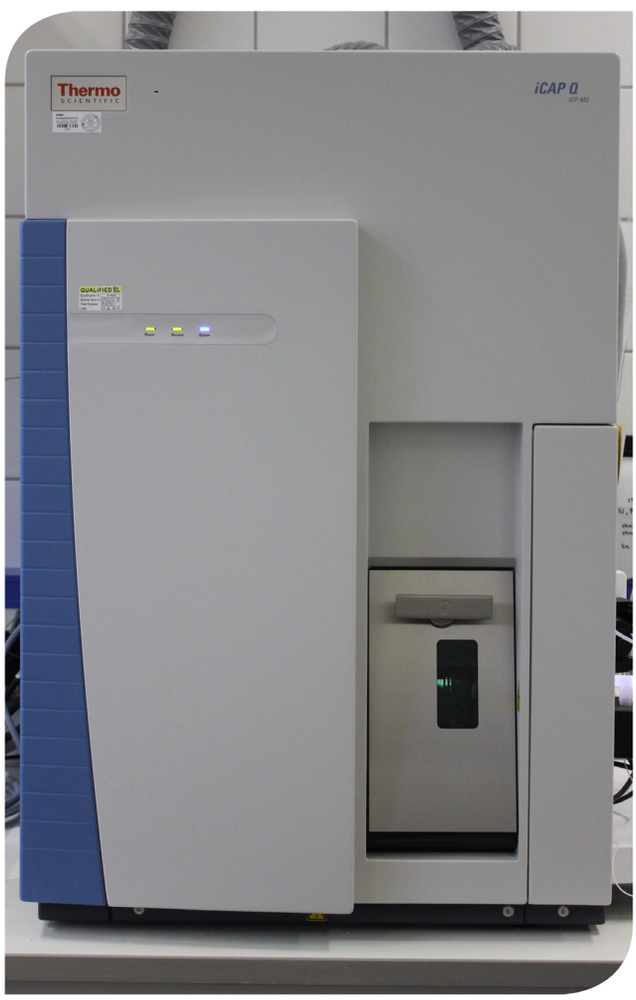
EP 5.20 (Metal catalysts or metal reagent residues) establishes limit values for 14 elements from metallic catalysts or reagents. Determination method requirements are regulated in EP 2.4.20 (Determination of metal catalysts or metal reagent residues).

The new regulations apply to all substances intended for pharmaceutical use, whether monographed or not. They will be binding as of September 2018, until which time transitional rules will be in effect for existing products.

USP <232> and <233>

The non-selective and interference-susceptible visual heavy metals testing procedure per USP <231> (Heavy Metals) is now outdated, being over 100 years old. For all new approvals in the US, the new chapters USP <232> (Elemental Impurities Limits) and USP <233> (Elemental Impurities Procedures) are already in place. This testing will become mandatory in January 2018 for release studies of existing approvals and for all monographed active and inactive substances.

In these chapters, limit values are set for 15 elements in pharmaceutical products and examination by means of ICP/MS and ICP/OES established as a standard method. The scope of testing is determined in a risk assessment of the elements that could be naturally found in, added to or unknowingly end up in the final product. Therefore, analysis of all 15 elements is not necessarily required.





Our Offering

We support you with our ICP/MS portfolio in documenting your products' conformity with the new guidelines:

Qualitative ICP/MS screening

A helpful risk assessment tool for the manufacturing process that gives you a quick overview of the presence or absence of many elements at low cost. This allows identification of elements of interest that can then be quantified as required.

Quantitative ICP/MS screening

Highly effective for obtaining an initial overview of content levels of specific elements. In the risk assessment process, for example, elements subject to control can be monitored to ensure they remain below a warning limit.

Element determination according to …

ICH-Guideline Q3D ("Elemental Impurities")

USP <730> ("Plasma Spectrochemistry")

USP <232> ("Elemental Impurities – Limits"),
USP <233> ("Elemental Impurities – Procedures")

EP 2.2.58 ("Inductively coupled plasma-mass spectrometry")

EP 5.20 ("Metal catalysts or metal reagent residues"),
EP 2.4.20 ("Determination of metal catalysts or metal reagent residues")

Our method allows precise determination of element content in conformance with the above regulations.

Matrix validation

Both EP and USP require matrix validation to be performed to establish that the analysis method is specifically usable for the respective matrix. In the respective monographs there are precise specifications regarding the parameters to be conformed with. We would be glad to advise you in this area and send you a testing proposal.

Why work with Eurofins?

We have more than 90 years of experience as a drug testing service provider, and have been GMP certified for over 20 years.

We are your one stop for the entire spectrum of services, including chemical and microbiological testing of active and inactive substances, herbal medicines, cosmetics and additives.

Any analyses we do not perform ourselves we outsource to the of over 375 laboratories in our worldwide network, putting 130,000 different methods at your disposal to meet your analytical requirements. Of course, we handle all the coordination for you. You can contact our experts directly at any time for an advice consultation.

Quality

All incoming packages are immediately registered before they are unpacked. Samples are first checked for integrity and storage conditions, then registered in our lab system. From this time, each sample container is uniquely marked with a barcode. Every procedural step is subject to four-eyes-principle.

We would be pleased to send you a draft of our Quality and Service Agreements.

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Our determination limits

Element	Included in			Our determination limits	
				Quantitative screening	Individual determination*
	ICH Q3D	USP <232>	EP 5.20	[µg/g]	[µg/g]
Li	x			0.2	0.2
V	x	x	x	0.2	0.2
Cr	x	x	x	0.2	0.2
Mn			x	0.2	0.02
Fe			x	2	2
Co	x			0.2	0.02
Ni	x	x	x	0.2	0.2
Cu	x	x	x	0.2	0.2
Zn			x	2 / 10 **	2 / 10 **
As	x	x		2	0.02
Se	x			2	2
Mo	x	x	x	0.2	0.2
Ru	x	x	x	0.2	0.02
Rh	x	x	x	0.2	0.02
Pd	x	x	x	0.2	0.02
Ag	x			0.2	0.2
Cd	x	x		0.2	0.02
Sn	x			0.2	0.2
Sb	x			0.2	0.02
Ba	x			0.2	0.2
Os	x	x	x	0.2	0.02
Ir	x	x	x	0.2	0.02
Pt	x	x	x	0.2	0.02
Au	x			0.2	0.2
Hg	x	x		0.2	0.02
Tl	x			0.2	0.02
Pb	x	x		0.2	0.02

* according to system-validated standard methods. Please contact us to discuss your specific needs.

** without/with microwave pressure digestion

Services

Chemistry/Biochemistry
Cell Banking Services
Facility & Process Validation
GMP Manufacturing
Method Development & Validation
Microbiology
Molecular & Cell Biology
Raw Materials Testing
Release Testing
Stability Testing & Storage
Viral Clearance & Viral Safety
Professional Scientific Services®

With more than 25 Laboratories in 13 countries, Eurofins BioPharma Product Testing is the largest network of harmonized bio/pharmaceutical GMP product testing labs worldwide.

www.eurofins.de/heavy-metals