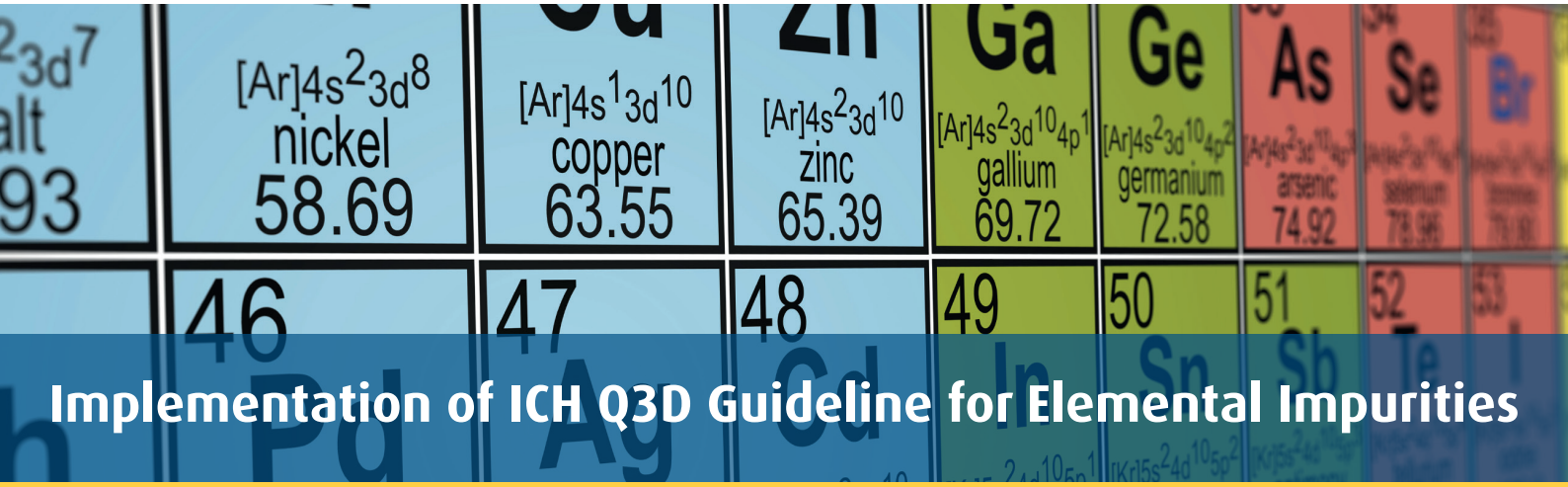

Implementation of ICH Q3D Guideline for Elemental Impurities

The ICH Q3D guideline presenting a policy for limiting metals in drug products and pharmaceutical ingredients has now reached step 5 - the implementation stage. ICH Q3D applies to new finished drug products entering the market and new products containing existing drug products.

ICH Q3D has been adopted by CHMP and comes into effect for new marketing authorization applications in June 2016. For existing medicinal products, the corresponding date is December 2017. USP has also aligned the effective date for their corresponding chapters, <232> and <233>, setting the date to 1 January 2018.

What does this mean?

There is little time to waste for the pharmaceutical industry. The new Elemental Impurities guidelines should already be considered in the development of new drug products. Furthermore, plans for assessing risks and measuring metals in existing products should be highly prioritized. The guideline lists 24 elements with corresponding PDEs recommended for consideration in the risk assessment.

Sources of elemental impurities

There are numerous potential sources of elemental impurities in the manufacturing process of drug products. While the most significant risk comes from intentionally added metal catalysts, other sources such as manufacturing equipment, solvents, water and reagents should also be considered. Particularly challenging is assessing the potential contribution of elemental impurities from excipients. Environmental factors will have a significant impact meaning the source of the excipient is important to consider. Figure 1 shows the elements included in ICH Q3D, and gives examples of potential sources for each element.

How can ALS Scandinavia help?

ALS Scandinavia offers tailor-made screening analyses for client-specific needs, from a single element to packages of all elements included in ICH Q3D, USP <232>, or even up to 70 elements in a single certificate of analysis. In the risk assessment process, non-validated analytical methods may be used. The results can thereafter be used for deciding on which elements to test for on a regular basis using a validated method.

ALS has successfully completed well over 100 method validations compliant with ICH Q2 (R1), USP <233> and Ph.Eur. 2.4.20 for clients in the pharmaceutical industry.

Our laboratory holds 11 ICP-SFMS (high resolution ICP-MS) instruments. Combined with decades of experience with ICP-techniques and method validations, this makes ALS Scandinavia a reliable partner with solid backup capacity; ***right solutions, right partner.***

Figure 1. Elements included in ICH Q3D

Element	Class	If intentionally added (all routes)	If not intentionally added		
			Oral	Parental	Inhalation
Cd (Cadmium)	1	Yes	Yes	Yes	Yes
Pb (lead)	1	Yes	Yes	Yes	Yes
As (arsenic)	1	Yes	Yes	Yes	Yes
Hg (mercury)	1	Yes	Yes	Yes	Yes
Co (cobalt)	2A	Yes	Yes	Yes	Yes
V (vanadium)	2A	Yes	Yes	Yes	Yes
Ni (nickel)	2A	Yes	Yes	Yes	Yes
Tl (thallium)	2B	Yes	No	No	No
Au (gold)	2B	Yes	No	No	No
Pd (palladium)	2B	Yes	No	No	No
Ir (iridium)	2B	Yes	No	No	No
Os (osmium)	2B	Yes	No	No	No
Rh (rhodium)	2B	Yes	No	No	No
Ru (rubidium)	2B	Yes	No	No	No
Se (selenium)	2B	Yes	No	No	No
Ag (silver)	2B	Yes	No	No	No
Pt (platinum)	2B	Yes	No	No	No
Li (lithium)	3	Yes	No	Yes	Yes
Sb (antimony)	3	Yes	No	Yes	Yes
Ba (barium)	3	Yes	No	No	Yes
Mo (molybdenum)	3	Yes	No	No	Yes
Cu (copper)	3	Yes	No	Yes	Yes
Sn (tin)	3	Yes	No	No	Yes
Cr (chromium)	3	Yes	No	No	Yes

Yes/no indicates recommendations as to whether an element should be included in the risk assessment.

Manufacturing equipment | Excipients | Metal catalyst

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