NEW USP AND PH.EUR LIMITS AND PROCEDURES FOR

Elemental impurities in pharmaceuticals

Both the USP and the European Pharmacopeia, Ph.Eur, have proposed to replace the old, wet chemistry heavy metals test with new procedures and limits using ICP-MS and ICP-OES (Inductively Coupled Plasma-Mass Spectrometry and ICP-Optical Emission) techniques. ALS Scandinavia specializes in trace elemental analysis with ICP instruments and has long experience working with the pharmaceutical industry. We can help you show compliance with both pharmacopeias without extensive instrument and personnel investments.

Changes to heavy metals test procedures for the analysis of pharmaceuticals are under review and are proposed to be implemented in May 2014. The test methodology currently described in the USP was first introduced over one hundred years ago. The test can be difficult to conduct, time consuming and can fail to detect some toxic elements.

USP chapter 231: Heavy Metals will be replaced by USP chapters 232: Elemental Impurities – Limits and 233: Elemental Impurities – Procedures. The new chapters are designed to set safer limits for public exposure and to reduce the environmental impact of the old method.

The proposed procedures focus on the use of ICP-MS and ICP-OES (Inductively Coupled Plasma-Mass Spectrometry and ICP-Optical Emission) and microwave digestion instrumentation. ICP-OES and ICP-MS are fast multielement techniques, capable of analysing as many as 70 elements in a 2-min run after sample digestion. These powerful techniques can identify and quantify each metallic impurity with higher sensitivity and selectivity than conventional precipitation-based detection methods. Required sample amounts for ICP-OES and ICP-MS can be as low as 20–50 mg with detection limits down to ppb or even ppt levels.

ALS Scandinavia's trace elemental laboratory in Sweden has a GMP certificate, FDA approval, is ISO 17025 accredited, and has a clean floor environment that houses 14 ICP instruments. ALS Scandinavia's extensive experience with microwave digestion and ICP-MS analysis will assist you prove compliance with the new "heavy metals" regulation changes. We can analyse all the elements mentioned in the new chapters at all limits. Choose the elements that are required for your product and we will put together a suitable analytical package for you.

Verification of the methods described in USP 233 will be required prior to use. With experience of validating around 80 substance-specific methods for the pharmaceutical sector, ALS Scandinavia can help you with this verification to meet the requirements of the new USP chapters on heavy metals.

Table 1. Elemental impurities for drug products (www.usp.org)

Element	Oral daily dose PDE[a] (µg/day)	Parenteral daily dose PDE (µg/day)	Inhalational daily dose PDE (µg/day)	LVP Component Limit (µg/g)
Cadmium	25	2.5	1.5	0.25
Lead	5	5	5	0.5
Inorganic arsenic	1.5	1.5	1.5	0.15
Inorganic mercury	15	1.5	1.5	0.15
Iridium	100	10	1.5	1.0
Osmium	100	10	1.5	1.0
Palladium	100	10	1.5	1.0
Platinum	100	10	1.5	1.0
Rhodium	100	10	1.5	1.0
Ruthenium	100	10	1.5	1.0
Chromium	*	*	25	*
Molybdenum	100	10	250	1.0
Nickel	500	50	1.5	5.0
Vanadium	100	10	30	1.0
Copper	1000	100	70	25

PDE[a] = Permissible daily exposure based on a 50 kg person.
*Not a safety concern

Find out more at: www.alsglobal.se/en

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