

## Analysis of elemental impurities in drugs



### Analysis of elemental impurities

To provide benefit to public health, it is envisioned that a safety-based approach would be taken for the control of metal impurities in drugs.

ICH (International Conference for Harmonisation) issued at the end of 2016 the guideline ICH Q3D for the control of elemental impurities. It's been primarily adopted by US (Chapter <232>/<233>), European and Japanese pharmacopoeias.

When elemental impurities are known to be present, have been added, or have the potential for introduction, assurance of compliance to the ICH Q3D levels is required.

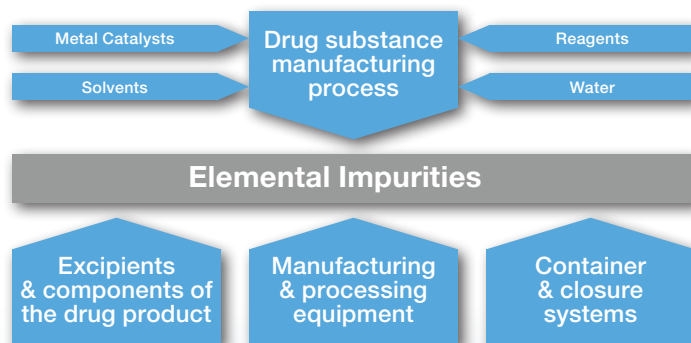


Figure 1: Elemental impurities sources in drug products

ICH Q3D has established allowed limits for 24 elemental impurities considered toxic or very toxic to humans. They have been placed into three classes based on their toxicity and likelihood of occurrence in the drug product. It defines the maximum permitted daily exposure (PDE) levels in µg/day for the major routes of administration.

Figure 2: Permitted Daily Exposures for Elemental Impurities

**Class 1:** Toxicants that have limited or no use in the manufacture of pharmaceuticals, but come from commonly used materials, and require evaluation during the risk assessment across all potential sources of elemental impurities and routes of administration.

Element	EDP µg/day		
	Oral	Parenteral	Inhalation
Cd	5	2	2
Pb	5	5	5
As	15	15	2
Hg	30	3	1

**Class 2A:** Route-dependent toxicants that have relatively high probability of occurrence in the drug product and thus require risk assessment across all potential sources of elemental impurities and routes of administration.

Element	EDP µg/day		
	Oral	Parenteral	Inhalation
Co	50	5	3
V	100	10	1
Ni	200	20	5

**Class 2B:** Route-dependent toxicants that have a reduced probability of occurrence in the drug product related to their low abundance and low potential to be co-isolated with other materials. They may be excluded from the risk assessment unless they are intentionally added to the drug substances, excipients or other components of the drug product.

Element	EDP µg/day		
	Oral	Parenteral	Inhalation
Tl	8	8	8
Au	100	100	1
Pd	100	10	1
Ir	100	10	1
Os	100	10	1
Rh	100	10	1
Ru	100	10	1
Se	150	80	130
Ag	150	10	7
Pt	100	10	1

**Class 3:** The elements in this class have relatively low toxicities by the oral route of administration but may require consideration in the risk assessment for inhalation and parenteral routes.

Element	EDP µg/day		
	Oral	Parenteral	Inhalation
Li	550	250	25
Sb	1200	90	20
Ba	1400	700	300
Mo	3000	1500	10
Cu	3000	300	30
Sn	6000	600	60
Cr	11000	1100	3

# Analysis of elemental impurities in drugs

Analysis of elemental impurities should be performed both in raw materials as well as in finished products.

Spectroscopic techniques as Induced Coupled Plasma combined with detection technologies, such as Optical Emission Spectrometry and Mass Spectrometry (ICP-OES or ICP-MS), or Graphite Furnace Atomic Absorption (GFAA) are the major control procedures for analyzing and quantifying trace concentrations of elements in a wide variety of samples.

Scharlab offers a wide range of products for this analysis, including standards and ultrapure reagents (acids, alkalis, water...), to guarantee optimum results when analyzing inorganic traces by any of the above-mentioned techniques.

✓ **Ultrapure Reagents (acids, bases and water)**

- Ultratrace ppb - certified at maximum element impurity levels of 1 part per billion
- Ultratrace ppt - certified at maximum element impurity levels of 100 part per trillion

✓ **ICP Standards according ISO 17025 and ISO Guide 34**

- Single element standards
- Multielement standards
- We offer a set of 3 Multielement ICP standards, covering the 24 metals, in concentrations proportional to the oral PDE µg/day, on the ICH Q3D guideline:

Description	Art. No.	Capacity
<b>ICP Multielement Standard 1 - ICH Q3D Oral, 10 elements in HNO<sub>3</sub> 12%</b> Ag 150mg/l; As 15mg/l; Cd 5mg/l; Co 50mg/l; Hg 30mg/l; Ni 200mg/l; Pb 5mg/l; Se 150mg/l; Tl 8mg/l; V 100mg/l	MU01220100	100 ml
<b>ICP Multielement Standard 2 - ICH Q3D Oral, 7 elements in HCl 10%</b> Au 100mg/l; Ir 100mg/l; Os 100mg/l; Pd 100mg/l; Pt 100mg/l; Rh 100mg/l; Ru 100mg/l	MU01230100	100 ml
<b>ICP Multielement Standard 3 - ICH Q3D Oral, 7 elements in HNO<sub>3</sub> 5% HF 0,5%</b> Ba 140mg/l; Cr 1100mg/l; Cu 300mg/l; Li 55mg/l; Mo 300mg/l; Sb 120mg/l; Sn 600mg/l	MU01240100	100 ml



Download here the Scharlab's product range for Elemental Impurities Analysis