SPI Pharma™
Making a Difference
An ABF Ingredients Company

The Importance of Elemental Impurities
Are You Prepared?

What are Elemental Impurities ("EI")?

Elemental Impurities are metallic element contaminants found in drug products, these contaminants may arise from several sources:

- Intentionally added during manufacturing
- Unintentionally picked up during the manufacturing process, through contact with processing equipment or by being present in raw materials, and are consequently detectable in the drug product.

Why are these impurities a problem?

- Elemental Impurities above established permitted daily exposure levels pose a risk to patient health due to toxicological effects while providing no therapeutic benefit.

My API's are USP/EP/JP monograph compliant, what has changed?

- Since Jan 2018, USP Chapter <232> Elemental Impurities—replaced Chapter <231> Heavy Metals and its reference in individual monographs is deleted. Chapter <232> is aligned with ICH Q3D guidelines. Numerous monographs still include specific Elemental Impurities with defined specifications
- The final product manufacturer is now responsible to manage the level of Elemental Impurities in the finished dosage form according to ICH Q3D guidelines
- API and excipient suppliers should assess materials consistent with ICH Q3D to enable final product manufactures to complete risk assessments and ensure compliance

Who developed the guidance for Elemental Impurities?

- The ICH (International Council for Harmonization) Association
- The ICH was originally founded in 1990 to promote public health through international harmonisation of levels of Elemental Impurities in final products - for regulators and the pharmaceutical industry
- ICH is comprised of 17 Members:
- ICH can be found on the web at: www.ich.org

Founding Regulatory bodies:
EC (Europe); MHLW/PMDA (Japan); FDA (US)

Founding Industries:
EFPIA (Europe); JPMA (Japan); PhRMA(US)

Health Agencies & Regulatory bodies:
Swissmedic (Switzerland);
Health Canada (Canada), ANVISA (Brazil);
NMPA (China); HAS (Singapore); MFDS (S. Korea);
TFDA, (Chinese Taipei); TITCK (Turkey)

Three Critical Questions You Need to be Asking Now.

1. Do you know what level of impurities you have in your finished dosage form?
2. Have you asked your supplier to provide you with data and a rigorous assessment of Elemental Impurities for their product supplied to you?
3. Will you have resources and time to reformulate and switch to alternative suppliers if ICH guidelines are adopted in the regions that you sell your product into?

You can rely on SPI.
Our APIs and excipients have been thoroughly tested with documented risk assessments so you can meet the limits for your finished dosage form

ICH guidelines for Elemental Impurities are being adopted globally at an extremely fast pace since 2018.

January 2018		July 2020	Implementation in progress
EC, Europe Swissmedic, Switzerland HSA, Singapore	Health Canada, Canada FDA, United States	NMPA, China	MHLW/PMDA, Japan ANVISA, Brazil MFDS, Republic of Korea TFDA, Chinese Taipei

The SPI Advantage

The API's and excipients supplied by SPI Pharma are within the established limits, giving you assurance that our materials will support compliance in the final product

Since 2018 SPI has been making substantial investments to ensure we are well prepared to support our customers to respond to the ICH Q3D requirements as global implementation progresses

- SPI substantially invests in state-of-the-art instrumentation and other resources to perform a thorough Elemental Impurities risk assessment
- SPI products are below the thresholds as defined by individual monographs or ICHQ3D. Our customers avoid the cost and burden of incoming raw material testing because they know they can depend on our certifications.
- Our EI assessment reports clearly show how our products will enable customers to meet all ICH limits for Elemental Impurities.

What guidance does the ICH provide?

- ICH Q3D is a quality guideline for the control of Elemental Impurities in drug products (medicinal products), and it establishes Permitted Daily Exposures (PDEs) for 24 Elemental Impurities for drug products administered by the oral, parenteral and inhalation routes of administration.

Elemental Impurities Limits* in Finished Dosage Form

Elemental Impurities above permitted daily exposure poses a risk

Element	Class	Oral Concentration µg/g
Cd	1	0.5
Pb	1	0.5
As	1	1.5
Hg	1	3
Co	2A	5
V	2A	10
Ni	2A	20
Tl	2B	0.8
Au	2B	10
Pd	2B	10
Ir	2B	1010
Os	2B	10
Rh	2B	10
Ru	2B	10
Se	2B	10
Ag	2B	10
Pt	2B	10
Li	3	55
Sb	3	120
Ba	3	140
Mo	3	300
Cu	3	300
Sn	3	600
Cr	3	1100

If not intentionally added any of the above 24 EIs - those in Red box are required for risk assessment in orally administered products

* Based on a daily dose of not more than 10 gms/day

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