Mérieux NutriSciences

Elemental impurities
method validation & verification strategies

The term “Elemental Impurity” (EI) refers to **24 elements present in the environment, or used or intentionally introduced in the manufacturing of drugs or excipients**. Elemental impurities need to be monitored in drugs because they may **be toxic**, **interfere with drug stability** and **shelf-life**, and cause **unwanted side effects** to humans.

Determination of elemental impurities in active pharmaceutical ingredients, medicinal products, and raw materials, plays a **crucial role in pharmaceutical development and manufacturing**. The implementation of a **strategic approach in compliance with ICH Q3D and USP requirements is imperative** to ensure safety and quality of drug substances or finished drug products.

Challenges introduced by the ICH Q3D guideline

Identification of toxicologically relevant Permitted Daily Exposure (PDE) limits
for individual elements - a substance-specific dose that is unlikely to cause adverse effects to the individuals who are daily exposed to this dose or lower, during their life

Risk-based approach
to assess the likelihood of elemental impurities being present in drug products

Inductively Coupled Plasma (ICP)
new analytical methodology setting new, specific limits for individual elements and replacing the wet chemical “heavy metals” limit test

MxNS capability testing strategies

In MxNS Chemical pharma labs, two testing options are available for **Elemental Impurities determination**:

1 TESTING OPTION

Method Validation Strategies

MxNS Chemical **establish**, **conduct**, **and authenticate a distinct procedure** for each specimen following the directives for elemental impurities. Furthermore, an analysis of **three separate batches will be executed to fulfill the risk evaluation** mandates stipulated by ICH Q3D. Such a strategy facilitates the provision of an analysis certification for standard issuance and batch testing.

2 TESTING OPTION

Method Suitability and Verification Strategies

MxNS Chemical has developed a **proprietary screening technique** on the specimen to evaluate its appropriateness for **identifying elemental impurities within the particular sample context**. Following an initial examination, this technique will be employed to scrutinize the elemental impurities across three separate batches to finalize the risk evaluation as mandated by ICH Q3D. Fields of application:

- **Non GMP** - Suitability verification of official/in-house validated methods applied to preliminary screening test;
- **GMP** - Suitability verification of methods validated on worst case products and applied to similar products.

EXPERTISE & KNOW-HOW

- More than **20 years' experience** in elemental analyses
- Routine **determinations of EIs (>800 samples/day)** in a wide range of matrices:
  - active pharmaceutical ingredients (APIs) & drug products
  - excipients, additives and raw materials
  - food supplements (including OTC products)
  - cosmetics
  - medical devices
  - packaging and containers, food products, environmental samples (air, water, soil)

Analytical techniques

- 14 ICP-MS
- 4 ICP-OES
- 1 IC-ICP-MS
- 3 AA with graphite furnace and hydride system
- 2 XRF
- 2 SEM-EDX

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