Imminent guidelines for measuring elemental impurities in drug products

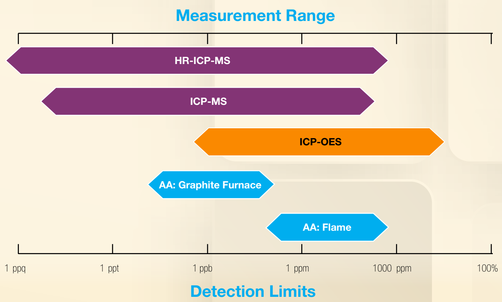
Select the Right Technique for Metals Analysis in your Pharma QA/QC Lab

The USP (United States Pharmacopeia) will soon be implementing new guidelines for measuring elemental impurities in drug products sold in the United States. Selecting a technique to use in your laboratory for Chapter <232> and <233> compliance requires consideration of these criteria:

1. Detection limits and measurement range **2.** Analysis speed **3.** The economics of ownership

Detection limits and measurement range

Consider the required detection limits for metals you will need to analyze. Will one technique cover all the metals you need to test, or will you require multiple techniques?

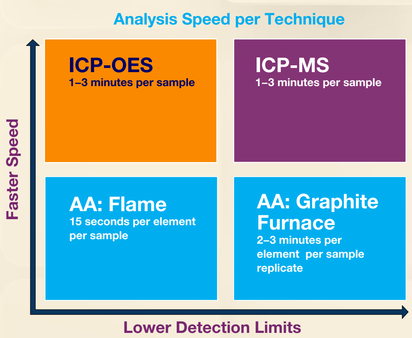


Element	Daily Dose Permitted Daily Exposures µg/g	Large Volume Parenteral Component Limit µg/g
Compulsory elemental impurities		
Inorganic Arsenic	15	0.15
Cadmium	5.0	0.05
Lead	10	0.1
Inorganic Mercury	15	0.15
Elemental impurities (if used in the drug manufacturing process)		
Chromium	250	2.5
Copper	2500	25
Manganese	2500	25
Molybdenum	250	2.5
Nickel	250	2.5
Palladium	100	1.0
Platinum	100	1.0
Vanadium	250	2.5
Osmium	100 (combination not to exceed)	1.0 (combination not to exceed)
Rhodium		
Ruthenium		
Iridium		

- The first 4 elements are mandatory. All laboratories must analyze for them.The remaining 12 elements must be analyzed if a laboratory uses them during their drug manufacturing process.
- The maximum Permitted Daily Exposure (PDE) is outlined for the two methods by which drugs are administered: enteral (oral, sublingual, rectal) and parenteral (intravenous) and is calculated based upon the recommended daily dosage for the drug.
- J: The concentration (w/w) of the element(s) of interest at the Target Limit, appropriately diluted to the working range of the instrument.
- Calibration and validation solutions must be prepared at concentrations that are at multiples of the calculated "J" value.

Analysis speed

Consider the analysis time for each technique, and the number of samples you will need to test in a day. Which technique will fit into your production timelines? Does the same technique that supports your timeline also support the detection limits you require?



Why the speed differences?

The analysis speed is related to how each technique works.

AAS (atomic absorption spectroscopy)

- Liquid samples are desolvated, vaporized, and atomized with either a flame or a graphite furnace.
- The gaseous atoms pass through a beam of light that is emitted from a radiation source at a single wavelength.
- The element for that wavelength absorbs an amount of light directly related to the concentration of the element in the sample. The process is repeated for each element.

ICP-OES (inductively coupled plasma – optical emission spectroscopy)

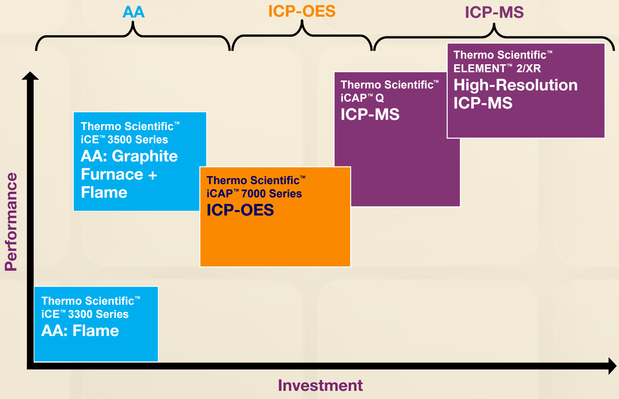
- Liquid samples are desolvated, vaporized, atomized, and excited in an argon plasma.
- When the excited atoms relax back to the ground state, they emit characteristic wavelengths of light.
- A solid state detector collects all the emitted wavelengths of light simultaneously.
- For each wavelength, the amount of emitted light is directly proportional to the concentration of the element in the sample.

ICP-MS (inductively coupled plasma – mass spectrometry)

- Liquid samples are desolvated, vaporized, atomized, and ionized in an argon plasma.
- Each element has a different mass; once ionized, each element forms its own characteristic mass spectrum.
- An ion counting detector counts the number of ions at each mass-to-charge ratio, which is directly proportional to the concentration of each element in the sample.

The economics of ownership

The instrumentation you select must also work within your lab's budget. Not just your budget for the initial purchase, but also for maintenance, consumables, training, and service. When you consider overall instrument performance (detection limits, linearity, target analytes) as well as your timelines and budget, which technique is right for your lab?



Need help?

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