WEBINAR

HEAVY METALS TESTING: Considerations for an ICP Analysis of the Big Four

THURSDAY, NOVEMBER 11
9:00–10:00AM EST

SPEAKERS:

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Heavy Metals Testing: Considerations for an ICP Analysis of the Big Four

- Overview of Heavy Metals Testing
  - Impacted Industries
  - Current Regulations
  - Current Events
  - Future
- Overview of Issues
  - Instrumental
  - Working solution(s)
  - Sample Prep
- Summary
  - IV Products
  - Technical Support

Overview of Heavy Metal Testing

- Impacted Industries
  - Everyone!
- Current Regulations
  - USP 232
  - US EPA
  - Consumer Product Safety Act (CPSA)
    - ASTM Standard F963-17 [<25 ppm As, <60 ppm Hg, <75 ppm Cd, and <90 ppm Pb]
  - FDA
    - Hg in fish [1 ppm] & cosmetics [1 ppm]
    - Color additives in cosmetics [3 ppm As]

Overview of Heavy Metal Testing

- Current Regulations (continued)
  - Mercury-Containing and Rechargeable Battery Management Act
    - Button Cell batteries [25 ppm Hg]
    - Rechargeables [Pb & Cd]
  - RoHS
    - EU directive that is shaping policy in the US
    - 10 substances regulated [Cd < 100 ppm; Pb & Hg < 1000 ppm]
  - Model Toxics in Packaging Legislation
    - Focuses on product packaging [Cd, Hg, & Pb < 100 ppm by weight]
  - CA Proposition 65
    - List of restricted chemicals
    - Maximum concentrations vary by product

Overview of Heavy Metal Testing

- Current Events
  - Baby rice cereal
    - Voluntary recall
    - Samples exceed limit for inorganic arsenic (100 ppb)
    - October 8, 2021
  - Furniture
    - Recall
    - Surface paint exceeds the limit for Pb (90 ppm)
    - October 28, 2021
- Future – more testing!

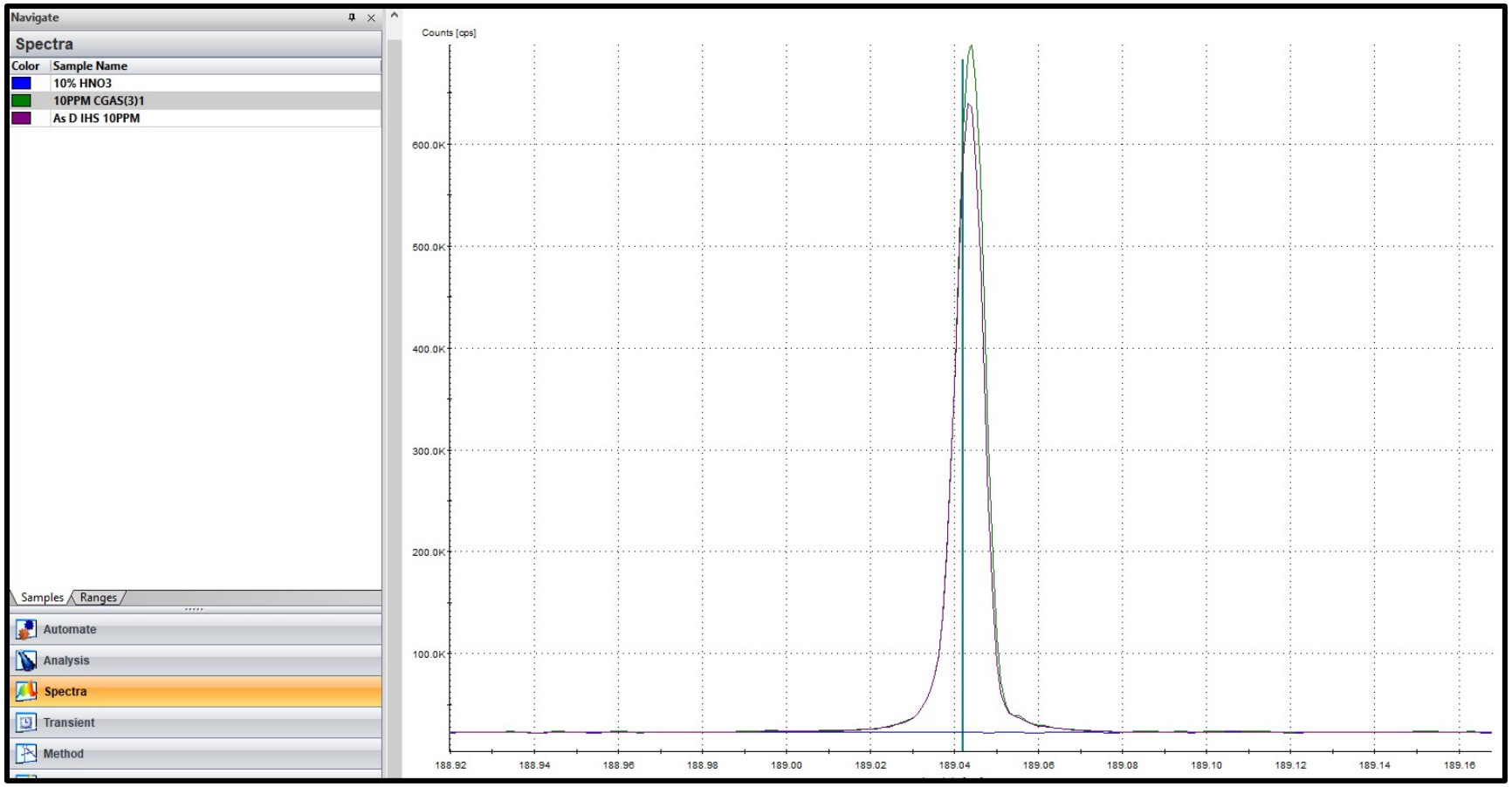
Overview of Issues

- Instrumental – spectral and mass interference(s); washout
- Working solution(s) – stability and compatibility
- Sample Preparation

Instrumental Issues: Arsenic

- Has no cationic chemistry (As(III) will exist as arsenite, As(V) will exist as arsenate)
- The oxidation state of As **DOES** influence the intensities obtained using ICP-OES.
- There are inconsistencies regarding which form of As, (III) or (V), gives higher intensities on ICP-OES, but in our observations, As(III) gives higher intensities.

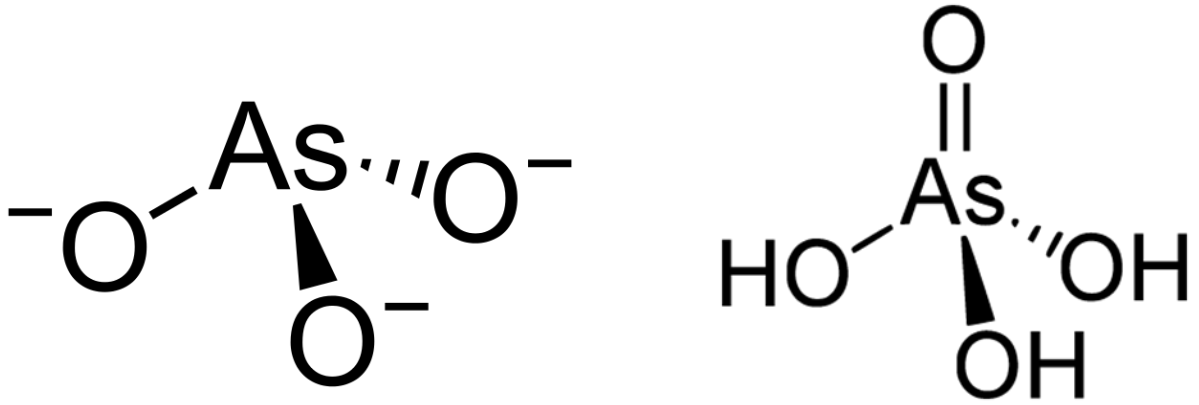
Instrumental Issues: Arsenic



- The green line is 10ppm As(III)
- The purple line is 10ppm As(V)

Instrumental Issues: Arsenic

- It is important to note the starting material used for your As standards (As metal, As_2O_3, As_2O_5), as this will affect the form of As in solution.
- Ensure that the As species is the same in your standards as in your samples (As(III) or As(V))



Instrumental Issues: Arsenic

Atomic Spectroscopic Information: (red text indicates severe at ~ concs.)

Technique / Line	Estimated D.L.*	Order	Type	Interferences
ICP-OES 189.042 nm	0.05/.005 µg/mL	1	atom	Cr
ICP-OES 193.696 nm	0.1/.01 µg/mL	1	atom	V, Ge
ICP-OES 228.812 nm	0.1/.01 µg/mL	1	atom	Cd, Pt, Ir, Co
ICP-MS 75 amu	30 ppt	n/a	M^+	$^{40}Ar^{35}Cl$, $^{59}Co^{16}O$, $^{36}Ar^{38}Ar^{1}H$, $^{38}Ar^{37}Cl$, $^{36}Ar^{39}K$, $^{150}Nd^{2+}$, $^{150}Sm^{2+}$

*ICP-OES D.L.'s are given as radial / axial view

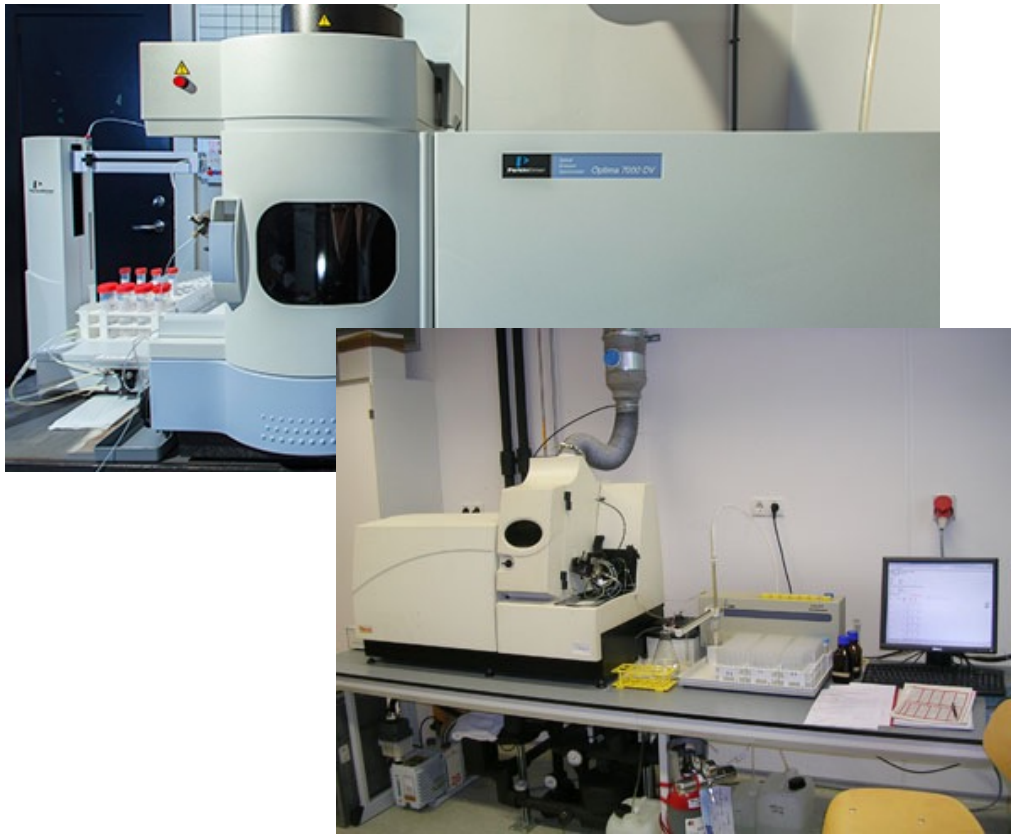
- The 189.042nm wavelength is usually the best line.
- Always check multiple lines to make sure they agree.
- Major Cd interference on 228.812nm wavelength. Do not use this line if Cd is present.
- If chloride is present, there will be a major interference from ArCl on ICP-MS
  - Use collision cell technology (He mode), if possible, to break up chloride interferences.

Instrumental Issues: Mercury

- **Hg MUST be in the Hg^{+2} form for accurate ICP measurements!**
- Hg sticks to plastic in HNO_3 matrices → many intro system components are composed of plastic!
- Glass intro system preferred for Hg
- Initial analyses should not be affected, however memory effects due to Hg washing out over time can affect subsequent analyses.
  - Thiourea or higher HCl rinses can help with washout issues
- Best stabilized in HCl. Chloride will cause interferences for As and Se on ICP-MS
  - Use collision cell (He mode) to break up interferences

Instrumental Issues: Mercury

- Hg_2^{2+} can be converted to a mix of Hg^{2+} and Hg^0 in the presence of chloride or other ligands.
- If Hg is present, even in small part, as the metallic (Hg^0) species, the nebulization/transport efficiency will be significantly higher for Hg and signal could increase several hundred percent.
- Extremely high recoveries → reduced Hg species
- Low results → Hg loss due to adsorption or precipitation of Hg_2^{2+} with chloride



Instrumental Issues: Mercury

Atomic Spectroscopic Information: (red text indicates severe at ~ concs.)

Technique / Line	Estimated D.L.*	Order	Type	Interferences
ICP-OES 184.950 nm	0.03/.005 µg/mL	1	atom	
ICP-OES 194.227 nm	0.03/.005 µg/mL	1	ion	V
ICP-OES 253.652 nm	0.1 /.03 µg/mL	1	atom	Ta, Co, Th ,Rh , Fe, U
ICP-MS 202 amu	9 ppt	n/a	M^+	$^{186}W^{16}O$

*ICP-OES D.L.'s are given as radial / axial view

Additional preferred lines:
ICP-OES: 435.835 nm
ICP-MS: 199amu, 200amu, *201amu (best line if W is in the sample, do not use if Re is in sample)

Instrumental Issues: Cadmium

Atomic Spectroscopic Information: (red text indicates severe at ~ concs.)

Technique / Line	Estimated D.L.*	Order	Type	Interferences
ICP-OES 214.438 nm	0.003/.0003 µg/mL	1	ion	Pt, Ir
ICP-OES 228.802 nm	0.003/.0003 µg/mL	1	atom	Co, Ir, As, Pt
ICP-OES 226.502 nm	0.003/.0003 µg/mL	1	ion	Ir
ICP-MS 111 amu	11 ppt	n/a	M^+	$^{95}Mo^{16}O$

*ICP-OES D.L.'s are given as radial / axial view

*Major As interference on 228.802nm wavelength. Do not use this line if As is present.

- Other recommended masses: 112 and 114amu

Instrumental Issues: Lead

Atomic Spectroscopic Information: (red text indicates severe at ~ concs.)

Technique / Line	Estimated D.L.*	Order	Type	Interferences
ICP-OES 168.215 nm	0.03/.003 µg/mL	1	ion	Co
ICP-OES 220.353 nm	0.04/.006 µg/mL	1	ion	Bi, Nb
ICP-OES 217.000 nm	0.09/.03 µg/mL	1	atom	W, Ir, Hf, Sb, Th
ICP-MS 208 amu	5 ppt	n/a	M^+	$^{192}Pt^{16}O$, $^{192}Os^{16}O$

*ICP-OES D.L.'s are given as radial / axial view

- Additional masses: 204 (Hg, Os, and Yb interference), 206 (Pt and Os interferences), and 207amu (Ir interference)

Instrumental Issues

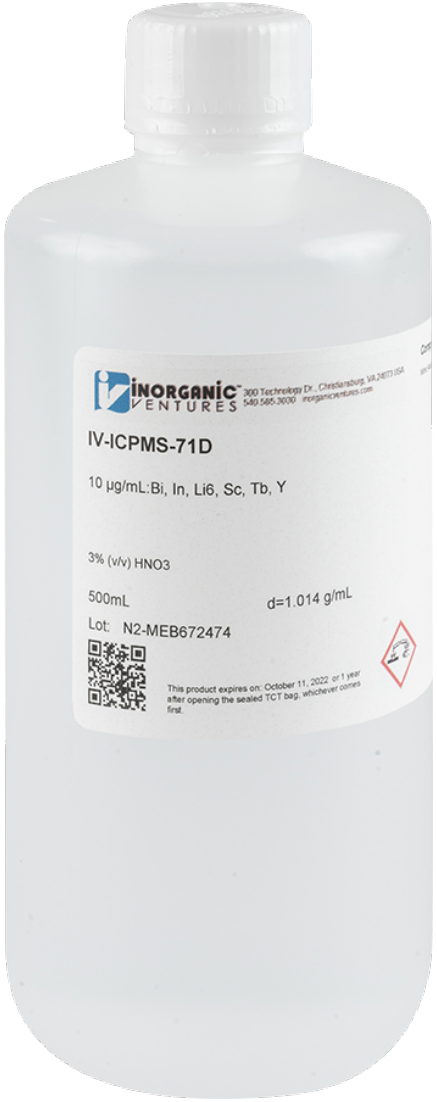
- Salting out may be an issue for high salt matrices.
  - Cone conditioning prior to analysis may be necessary
  - Or you may need to dilute samples further
  - Aerosol dilution can be used, if available, to dilute sample before introducing to the plasma
- Corrosion of instrument components due to high acid
- Clogging of the nebulizer
  - Contact instrument manufacturer regarding TDS limitations and other limitations of your particular instrument

Instrumental Issues

- **Matrix matching** samples and standards is very important for achieving accurate results.
  - Account for spectral interferences
  - Account for signal suppression from high matrix
  - Ensure consistent nebulization efficiency between samples and standards
- If the solutions and standards can not be matrix-matched, **standard additions** is a great method to account for matrix effects.
  - More information: https://www.inorganicventures.com/icp-guide/standard-addition-internal-standardization-and-isotope-dilution

Instrumental Issues

- **Internal Standards** can help correct nebulization or plasma related effects. Choose an internal standard that:
  - Is not contained in the sample (lanthanides are common, but should be avoided if fluoride is present)
  - Is stable in the solution (compatible with matrix and other elements)
  - Gives sufficient signal to noise ratio
  - Behaves similarly in the plasma
  - Will not have interferences from other elements in the sample or interfere on other analytes
  - Has a mass similar to the analyte of interest (for ICP-MS)
    - If there are multiple analytes, multiple internal standards may be necessary to cover the desired mass range.
    - The most common internal standards are ^{6}Li, Sc, Y, In, Tb and Bi.
  - https://www.inorganicventures.com/catalogsearch/result/?q=internal%20standard

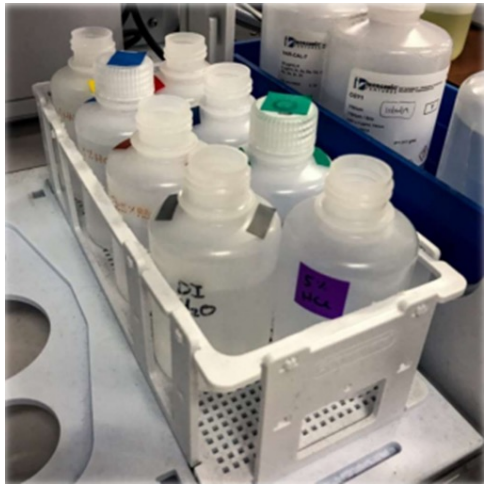


Instrumental Issues

- **Reference Materials:** use a well-characterized material that is similar to your sample that can be used to validate your method
  - Are you getting the correct results for each analyte in the RM using your method?
  - Is anything being lost?
- **Run Method Blanks!** This will help determine whether contamination is being introduced.

Instrumental Issues: Washout

- Of the Big Four, **Hg** is going to be the one that has washout issues
- For OES, we recommend reconditioning the spray chamber surface with RBS^{TM}-25 (2.5%) → will make the surface less “sticky”
  - Not recommended for MS (high Na)
- Sample tubing is the main issue for Hg sticking (especially PVC tubing)
- HCl / Thiourea
  - 1-10% v/v HCl
  - 0.5% w/v Thiourea
  - Also good for Au
- NH4OH
  - 1-5% v/v for OES or MS



- *If Triethanolamine (TEA) has been used for HF neutralization in a prior analysis, make sure to switch out your waste solution before Hg analysis as Hg can be reduced to Hg^0 and travel back up the lines to the instrument causing memory effects

Working Solutions Issues

- Pb is a common contaminant in pipet tips and acid reagents (HNO_3)
- Keep in acid matrix!
- Avoid neutral/basic media
  - Many cationic metals may form insoluble arsenates when mixed with As under pH neutral conditions.
  - Cd can form insoluble carbonate and hydroxide.
  - Pb can form insoluble carbonate, borate, sulfate, sulfite, sulfide, phosphate, oxalate, chromate, tannate, iodate, and cyanide
  - Hg can form insoluble carbonate
- Avoid mixing Pb with Cr^{+6} and H_2SO_4
- Avoid mixing Hg with tartrate, as Hg can be reduced to the metallic form.
- Cadmium chloride, bromide, and iodide are soluble in water.
  - *CdI_2 is one of the few iodides soluble in ethanol
- **All** Cd compounds are soluble in excess NaI, due to the formation of the complex ion, CdI_4^{2-}.

Working Solutions Issues

- As and Pb, along with Bi, can have issues when mixed at higher concentrations.
- If a solution contains any two of the following elements, As, Bi, or Pb, at concentrations greater than 500ppm, a higher acid matrix of at least 10% v/v HNO_3 may be needed to maintain stability.
- If As and Bi are both present at concentrations of 1000ppm or greater, then at least 15% v/v HNO3 is required.
- However, high acid concentrations can cause Pb to drop out as the nitrate, so be careful with the order of additions and do not add Pb to a concentrated HNO_3 environment.
  - Same issues exist for Ba and Cs.
- Pb can also precipitate in HCl. Pb at 500ppm or greater may need higher HCl for stability (recommend 20% v/v HCl or greater).

Working Solutions Issues

- Reducing environments can convert Hg^{2+} to the Hg_2^{2+} dimer or the metallic form.
- Hg_2^{2+} disproportionation into metallic mercury and Hg^{2+}: $Hg_2^{2+} \xleftrightarrow{Cl^-} Hg^0 + Hg^{2+}$
- Hg^{2+} can reduce to Hg_2^{2+} if NO_2 gases remain in the container from reaction/production process
- Adding HNO_3 and boiling can convert Hg_2^{2+} back to the Hg^{2+} (recertification may be required)

  $Hg^0 + HNO_3 \rightarrow Hg^{2+} + NO_2$(brown fumes) + xs HNO_3 + heat to expel $NO_2 \rightarrow Hg^{2+}$ + xs HNO_3

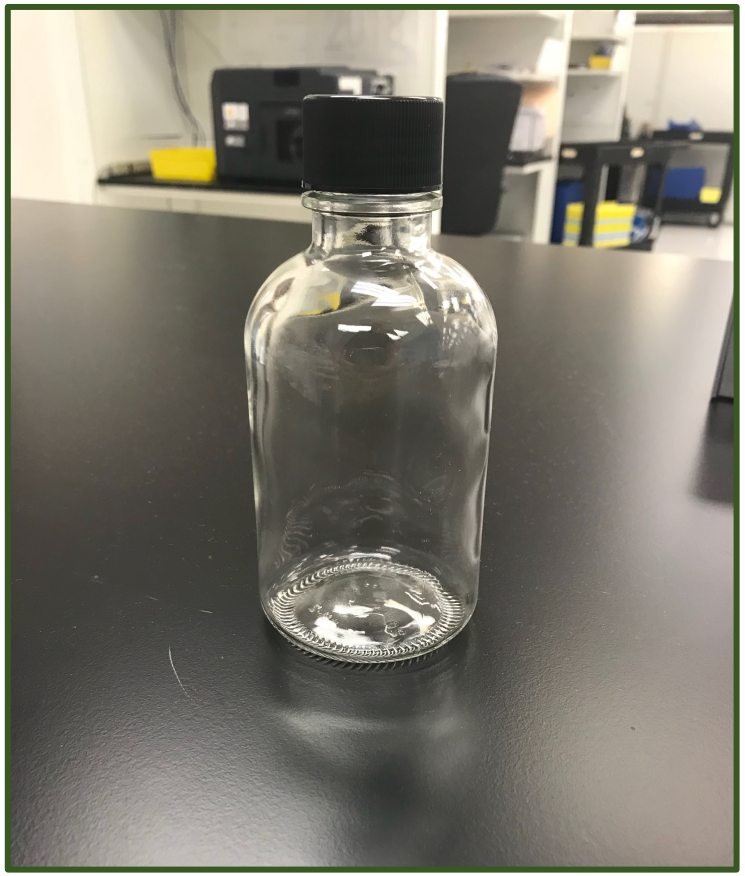
  $\rightarrow$ Dilute with H_2O to make stock products/concentrates

  $Hg^0 + HNO_3 \rightarrow Hg^{2+} + NO_2$ + xs $HNO_3 \rightarrow$ Dilute in $H_2O \rightarrow 2Hg^{2+} + NO_2 \rightarrow Hg_2^{2+} + H_2O$

  $Hg_2^{2+} + H_2O + HCl \rightarrow Hg^0 + Hg^{2+}$

- *Be Aware that boiling a solution containing As(III) with HNO_3 will oxidize As(III) to As(V)

Working Solutions Issues



- Hg in HNO3 matrix can adsorb to plastic container walls (~1ppm adsorbed)
- More of a concern for lower Hg concentrations (plastic not recommended for <200ppm Hg)
- Solution: May need to use borosilicate glass containers
- Solution concerns:
- Cannot have HF in standards contained in glass; HF is caustic to glass
- Glass has higher levels of contaminants than LDPE/HDPE
- Elements of concern: Al, Ba, B, Ca, Ga, Fe, Ni, K, Na, Sr, Zn, Zr

Working Solutions Issues

- Hg can be stabilized with $AuCl_3$ (generally 1ppm $AuCl_3$. See EPA bulletin:https://www.inorganicventures.com/pub/media/wysiwyg/files/mercury_preservation_techniques.pdf) or HCl.
  - Be aware of chloride interference for As and Se on ICP-MS.
  - $AuCl_3$ should be included in blanks, standards, and samples.
- HCl matrix is recommended
- If Ag is present, excess chloride will need to be added to keep Ag in solution and the solution will be photosensitive.
- If Tl is present, it should be in the Tl^{+3} state as Tl^{+1} may precipitate as the chloride

*There are also methods for stabilizing Hg with L-cysteine in dilute HNO3, but we have not used this methods in-house yet. (See Fresquez MR, Pappas RS, Watson CH. Establishment of Toxic Metal Reference Range in Tobacco from U.S. Cigarettes. J. Anal. Toxicol. 2013;37:298-304.)

Sample Preparation: Organic Sample Containing the Big Four

- Sample preparation technique will depend on the type of sample and the analytes of interest. Do you care about everything, or can some leftover insoluble be filtered out?
  - HF may be required to dissolve everything in the sample. (ex: Si, Ti, Sn, Sb, Zr, W, Ge, Ta, Hf, Nb)
- We recommend using a closed vessel or reflux condenser to prevent loss of volatile species
- Microwave digestion technique would be best
  - Use of HNO_3 and a small amount of HCl is recommended if analyzing for only As, Cd, Pb, and Hg. HCl needed to prevent Hg loss.
  - A small amount of H_2O_2 may need to be added to complete oxidation of certain organic species. For analysis of these four elements, it is not necessary/recommended.
  - *If H_2O_2 is used, always add H_2O_2 **LAST**, in very small increments, and proceed ***slowly*** and ***cautiously***!

Sample Preparation: Organic Sample Containing the Big Four

- Be aware of all contamination sources (use high purity DI water and acids, clean bottles/containers (we recommend LDPE), may need to leach materials, clean workspace, materials used to grind or blend the sample, etc.)
  - Prepare method blanks
- Avoid using glass or metal containers/materials at any point in the sample preparations process (contaminants)

Sample Preparation: Organic Sample Containing the Big Four

- Small sample size (~0.5g for cannabis)
  - Ensure that your samples are as homogenous as possible
- For sticky samples, may need to freeze before grinding

- Some possible methods:
  - EPA Methods: 200.7, 200.8, 6020A, 3052
  - USP 232/233 and ICH Q3D
  - FDA Methods 4.4 and 4.7
  - AOAC Methods 2015.01 and SMPR® 2020.001
  - Standard Methods 3030F
  - Many More!

Sample Preparation: Additional techniques for different sample types by element

Arsenic

- Metal: soluble in 1:1 H2O / HNO3
- Oxides: exist in crystalline and amorphous forms. The amorphoric form is more water-soluble. Most oxides typically dissolve in dilute acidic solutions when boiled.
- Minerals: 1 g of powered sample is fused in a Ni^0 crucible with 10 g of a 1:1 K_2CO_3 / KNO_3 mix, and the melt extracted with hot water
- Organic Matrices: 0.2-0.5 g of the sample are fused with 15 g of a 1:1 Na_2CO_3 / Na_2O_2 mix in a Ni^0 crucible. The fuseate is extracted with water and acidified with HNO_3.
    - Ensure that the mixture is covered with a layer of the 1:1 Na_2CO_3 / Na_2O_2 mixture to prevent loss of organoarsenic compounds
- As reacts with Pt, so a platinum crucible should be avoided for ashing.
- Zr crucibles should also be avoided to prevent loss of As due to formation of zirconium arsenate.
- If samples are made from arsenic trioxide, solution must be basic pH to dissolve into solution
- If standards are made from As metal, the solution must be heated with HNO_3 for at least 1 day after all metal has dissolved to convert all As to As^{+5}.
    - Take extra precaution when using this method to avoid build-up of H_2O_2 in the mixture → can lead to an explosion!

Cadmium

- Metal: soluble in HNO_3
- Oxides: soluble in HCl or HNO_3
- Ores: dissolve in HCl /HNO_3, then heat to fumes with H_2SO_4. The silica and lead sulfate are filtered off after the addition of water.
- Organic: dry ash at 450°C and dissolve ash in HCl
    - Cadmium chloride is volatile at temps over 400°C
- Alternative option: sulfuric / peroxide acid digestion:
    - Heat w/ conc H_2SO_4 to fumes, then add 30% H_2O_2 **dropwise** to finish oxidation
    - Make sure there is always an EXCESS of H_2SO_4
    - Be ***patient*** and proceed ***slowly***!

Sample Preparation: Additional techniques for different sample types by element

Mercury

- Use a closed vessel or condenser for acid digestions
- Avoid ashing! (Volatility and Toxicity of Hg^0)
- Metal or oxide: dissolve in HNO_3
- Organics: Extremely toxic! Please use extreme caution when working with organomercury compounds
    - Must be kept in solution with oxidizing agent to prevent loss as the metallic form!
    - Hg in biological material: heat with H2SO4 or HNO3 or both and potassium permanganate (in excess)
        - Oxidizing agent: permanganate
        - H2SO4 alone may not fully free all Hg
        - Use a closed vessel!
        - Low heat (~50-600C)
    - *Can also use perchloric acid instead of permanganate (For tips and safe use of perchloric acid and other acid digestions, please see Section 12 of our Trace Analysis Guide: https://www.inorganicventures.com/trace-analysis-guide/acid-digestions-of-organic-samples)

Lead

- Metal, Ores and Alloys: best dissolved in 1:1 H_2O / HNO_3
- Oxides: soluble in HNO_3, with the exception of PbO_2, which is soluble in HCl or HF
- Organic Matrices: dry ash and dissolve in dilute HCl.

Do not heat when dissolving to avoid precipitation of SiO_2.

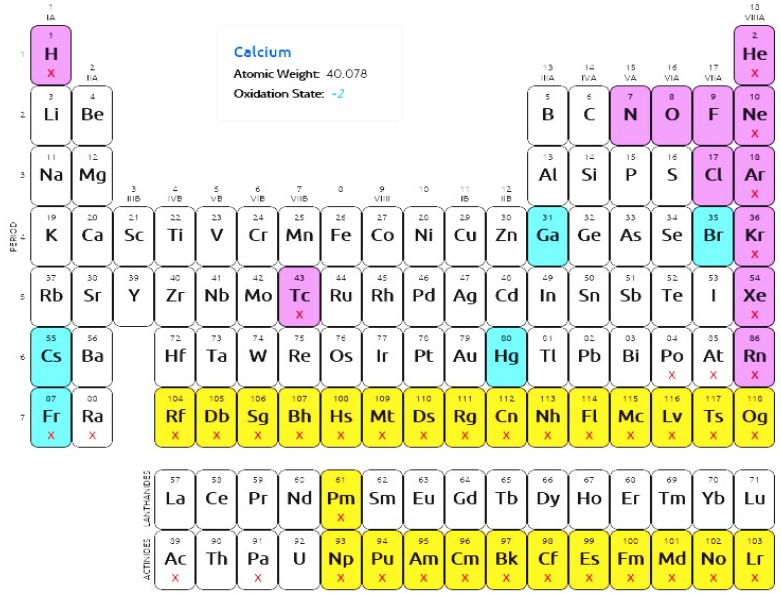
IV Products for Heavy Metal Testing

- Stock
  - IV-STOCK-65
    - USP <232> / ICH Q3D Class 1 Oral Elemental Impurities

30 µg/mL Hg
15 µg/mL As
5 µg/mL Cd & Pb

- Custom
  - Over 160 unique products containing As, Hg, Cd, and Pb

Technical Support – Available to Everyone
Online Resources at inorganicventures.com



Customers can visit our website's Tech Center, which includes:

- Interactive Periodic Table
- Sample Preparation Guide
- Trace Analysis Guide
- ICP Operations Guide
- Expert Advice
- And much, much more.