ICP-MS Interferences:
Types, Causes & Correction Strategies

A practical guide to recognizing spectral and non-spectral interferences, selecting appropriate correction strategies, and verifying analytical performance.

About the EPA Method Example in This Guide

The interference types and correction principles discussed in this guide apply across a broad range of ICP-MS methods and laboratory applications. EPA Method 200.8 is referenced throughout as a practical, publicly available example of how an established ICP-MS method addresses isobaric elemental overlaps, polyatomic ions, abundance-sensitivity effects, physical and matrix interferences, internal-standard correction and memory effects. Its repeated use is illustrative and does not mean that the guidance, correction strategies or CPI products discussed are limited to EPA Method 200.8 or to the analysis of water and waste samples.

Interference risks and appropriate correction strategies vary with the analytes, sample matrix, acid composition, instrument configuration and analytical method. Modern ICP-MS systems may also provide collision/reaction-cell, tandem mass-spectrometry and other capabilities not addressed identically in every method. Laboratories should follow the applicable analytical method, instrument documentation, validated SOPs and quality system when identifying, correcting and verifying interferences.

QUICK ANSWER

ICP-MS interferences occur when species other than the target analyte alter the signal measured at the selected mass-to-charge ratio, or when the sample matrix changes analyte transport, ionization, transmission, or detector response. Major categories include isobaric elemental overlaps, polyatomic ions, doubly charged ions, abundance-sensitivity effects, physical/matrix effects, and carryover. Correction depends on the mechanism and can include alternative isotope selection, mathematical correction, collision/reaction-cell operation, internal standardization, matrix matching, dilution, separation, instrument optimization, and method-specific interference checks.

Why ICP-MS Interferences Matter

ICP-MS combines multi-element capability with low detection limits, but the technique does not measure an element in isolation. The plasma, sample matrix, sample-introduction system, interface, ion optics, mass analyzer, and detector can all influence the signal that reaches the instrument software.

An interference can create a positive bias, suppress an analyte signal, increase background, destabilize internal-standard response, or make one isotope unsuitable for accurate measurement. The correct response is not simply to “apply an interference correction.” The analyst first needs to identify the likely mechanism, determine whether it is significant at the concentrations present, and use a correction strategy appropriate to the method and instrument.

EPA Method 200.8 provides a useful framework for ICP-MS interference control by addressing isobaric elemental interferences, abundance sensitivity, isobaric polyatomic ions, and physical interferences. Modern ICP-MS systems add collision/reaction-cell and, on some platforms, tandem mass-spectrometry approaches that can expand the options available to the laboratory.

The Major Types of ICP-MS Interference

The categories below are analytically distinct. Correct identification matters because a strategy that works for one class may have little effect on another.

Interference class	What happens	Typical response
Isobaric elemental	An isotope of another element occurs at the same nominal m/z as the analyte isotope.	Select another isotope when suitable; apply validated isotope-ratio correction; use separation or higher-resolution/tandem approaches when needed.
Polyatomic / molecular ion	Two or more atoms form an ion with the same nominal m/z as the analyte isotope.	Alternative isotope; collision/reaction cell; reaction chemistry; mathematical correction where validated; reduce precursor species or change sample preparation.
Doubly charged ion	A 2+ ion is detected at approximately half the isotope mass, creating an overlap at another analyte m/z.	Optimize plasma conditions; select another isotope; use cell/tandem-MS strategies where applicable; monitor formation ratios.
Abundance sensitivity	The tail or wing of a very intense neighboring mass peak contributes signal at an adjacent mass.	Optimize resolution/mass calibration; avoid problematic isotope where possible; reduce matrix or use separation.
Physical / matrix effect	The matrix changes aerosol formation, plasma behavior, ion extraction, transmission, or detector response relative to standards.	Internal standardization, matrix matching, dilution, robust plasma conditions, matrix removal or alternative sample preparation.
Carryover / memory	Residual analyte from a previous solution contributes to a later measurement.	Longer or chemically appropriate rinse, sequence optimization, contamination control, and reanalysis after carryover is removed.

1. Isobaric Elemental Interferences

An isobaric elemental interference occurs when isotopes of two different elements form singly charged atomic ions at the same nominal mass-to-charge ratio. A quadrupole ICP-MS operating at unit mass resolution cannot distinguish those species simply because their nuclei belong to different elements.

EPA Method 200.8 specifies that when an isobaric overlap is present, correction can be based on measuring another isotope of the interfering element and subtracting the appropriate contribution. The accuracy of that correction depends on the isotope ratio used and on the absence of additional unrecognized interference on the monitor isotope.

How to address an isobaric overlap

- Use an alternative analyte isotope if it provides adequate sensitivity and has fewer interferences.
- Use a validated isotope-ratio correction when the method and instrument configuration support it.
- Confirm that the isotope used to estimate the interferent is itself measured accurately.
- For difficult overlaps, consider matrix separation, higher mass resolution, reaction chemistry, or tandem ICP-MS if the laboratory's method permits those approaches.

2. Polyatomic Interferences

Polyatomic ions are among the most familiar ICP-MS spectral interferences. They consist of more than one atom and can be formed from argon plasma gas, water, acids, atmospheric gases, and sample-matrix components. If a polyatomic ion has the same nominal m/z as the analyte isotope, the mass analyzer may measure both together.

Common examples

Interfering ion	Potential analyte overlap	Analytical implication
40Ar16O+	56Fe+	Argon and oxygen-related species can create a signal at m/z 56.
40Ar12C+	52Cr+	Carbon-containing matrices can contribute to an overlap on chromium at m/z 52.
40Ar35Cl+	75As+	Chloride-containing matrices can create a well-known overlap on arsenic at m/z 75.
40Ar23Na+	63Cu+	High sodium matrices can contribute an argon-sodium polyatomic interference on copper.

The actual significance of a polyatomic interference depends on the sample matrix, acid composition, instrument conditions, analyte concentration, isotope selected, and interference-control mode. The presence of a theoretically possible ion does not automatically mean that it produces a significant bias in every method.

Collision/Reaction Cells: What They Do

Modern single-quadrupole ICP-MS instruments commonly use a collision/reaction cell between the interface and mass analyzer. In helium collision mode, kinetic energy discrimination can attenuate many larger polyatomic ions because they undergo more collisions with helium than monatomic analyte ions. Reactive gases use controlled ion-molecule chemistry to remove an interfering ion, move the analyte to a different mass, or otherwise separate analyte and interference behavior.

Collision/reaction-cell performance is interference-specific. Helium mode is broadly useful for many polyatomic species, but it does not resolve every elemental isobar or every doubly charged overlap. Reactive-gas methods can be highly effective, but the reaction pathway and potential product ions must be understood and validated for the analyte and matrix.

3. Doubly Charged Ion Interferences

ICP-MS normally measures singly charged positive ions, but some elements can also form doubly charged ions. A doubly charged ion has a mass-to-charge ratio equal to approximately half of its isotope mass, so it can overlap a singly charged analyte at that lower m/z.

Doubly charged ion formation is influenced by elemental ionization behavior and plasma conditions. Rare-earth elements are common examples of species that can produce analytically significant 2+ ions in some matrices.

Control options

- Monitor or verify doubly charged formation during instrument tuning when required by the method.
- Use robust plasma conditions and appropriate instrument optimization.
- Select a different analyte isotope if available and analytically suitable.
- Use validated cell or tandem-MS approaches when they address the specific overlap.
- Reduce or separate the interfering matrix component when instrumental correction is insufficient.

4. Oxide Ions and Other Matrix-Derived Molecular Species

Metal oxide ions such as MO+ can be formed in the plasma/interface and can overlap isotopes at higher masses. EPA Method 200.8 specifically notes matrix oxides such as TiO, ZrO, and MoO as potential interferences on elements including Ni, Cu, Zn, Ag, and Cd when the oxide-forming elements are present at sufficiently high concentrations.

Oxide formation is also used as an instrument-performance indicator because excessive oxide ratios can signal plasma or sample-introduction conditions that are not sufficiently robust. The appropriate tuning criterion is instrument- and method-specific.

5. Abundance Sensitivity and Adjacent-Mass Effects

Abundance sensitivity describes the contribution of the wings of a large mass peak to neighboring masses. This becomes important when a low-level analyte is measured adjacent to a much more intense ion signal.

EPA Method 200.8 identifies ion energy and quadrupole operating pressure as factors affecting abundance sensitivity and recommends recognizing wing-overlap effects and adjusting spectrometer resolution when necessary. In practice, good mass calibration, resolution verification, matrix control, and isotope selection help reduce risk.

6. Physical and Matrix Interferences

Not all ICP-MS interference is spectral. A sample can produce the correct ion at the correct mass and still yield biased results because its physical or chemical matrix behaves differently from the calibration standards.

Matrix effects can occur at several stages:

- Solution transport to the nebulizer, including viscosity-dependent uptake.
- Aerosol formation and transport, including effects of surface tension and dissolved solids.
- Atomization and ionization in the plasma.
- Ion extraction through the sampler and skimmer cones.
- Space-charge and ion-optics transmission effects.

- Deposition of dissolved solids on cones and other sample-interface components.

EPA Method 200.8 notes that high dissolved-solids levels can contribute to deposits on extraction and skimmer cones and states that dissolved solids not exceeding 0.2% (w/v) have been recommended to reduce such effects within that method context. That value should not be treated as a universal limit for every modern ICP-MS method or instrument.

Internal Standardization

Internal standards are introduced at controlled concentrations to help monitor and compensate for changes in signal caused by sample introduction, plasma behavior, ion transmission, and instrument drift. EPA Method 200.8 uses internal standardization and emphasizes selecting internal standards with behavior appropriate to the analyte and checking internal-standard response during analysis.

A stable internal-standard response does not prove that every spectral interference has been removed. Internal standards are particularly valuable for non-spectral and drift-related effects; they do not automatically correct an analyte-specific polyatomic or isobaric overlap.

Matrix Matching, Dilution and Sample Preparation

- Matrix matching can reduce differences between standards and samples when acid concentration or major matrix composition affects response.
- Dilution can reduce dissolved solids and matrix loading, but it also lowers analyte concentration and may compromise detection capability.
- Alternative digestion or preparation chemistry can reduce the formation of specific polyatomic precursors, but chemical stability and method requirements must be preserved.
- Separation or cleanup may be required when the matrix cannot be adequately controlled instrumentally.

7. Carryover and Memory Effects

Carryover is not a mass overlap, but it can mimic an interference because signal from a high-concentration sample persists into a subsequent blank, standard, QC solution, or sample.

EPA Method 200.8 directs analysts to consider memory effects when analyte concentrations appear to fall consecutively after a high sample and recommends reanalysis after an extended rinse when memory interference is suspected. Mercury is specifically noted as an element that can exhibit severe memory behavior.

Practical controls

- Use an appropriate rinse composition and sufficient rinse time.
- Sequence very high-concentration samples carefully.
- Monitor blanks following samples expected to create carryover.
- Clean or replace contaminated sample-introduction components when necessary.
- Reanalyze affected solutions only after carryover has been demonstrated to be controlled.

How to Diagnose an ICP-MS Interference

A systematic diagnosis is more effective than changing several instrument parameters at once.

Diagnostic step	What to evaluate
Confirm the symptom.	Is the problem a high blank, positive bias, low recovery, unstable internal-standard response, isotope disagreement, or calibration/QC failure?
Identify the likely interference class.	Ask whether the behavior is mass-specific (spectral), matrix-dependent (non-spectral), concentration-history dependent (carryover), or instrument-wide.
Check isotope behavior.	Where multiple analyte isotopes are available, compare results and expected isotope behavior. Disagreement can point to a spectral overlap.
Review the matrix.	Look for chloride, carbon, sulfur, phosphorus, high dissolved solids, unusually high major elements, or other precursors consistent with the observed interference.
Review internal-standard response.	Suppression or enhancement across internal standards can indicate matrix loading, transport, plasma, or ion-transmission effects.
Evaluate interference-control mode.	Check collision/reaction-cell gas, tuning, resolution, correction equations, and method-specific performance criteria.
Use an appropriate QC material.	Interference check standards and matrix spikes can help evaluate whether the analytical system is controlling relevant interferences.
Apply one validated corrective action at a time.	Then verify the change with standards/QC before interpreting sample data.

Choosing a Correction Strategy

The strongest correction is the one that addresses the actual mechanism without introducing a new bias.

Strategy	Best suited for	Key limitation
Alternative isotope	Avoids the interfering m/z entirely when another suitable isotope exists.	Sensitivity may be lower; alternate isotope can have its own interference.
Mathematical correction	Subtracts an estimated interferent contribution using another measured isotope or correction equation.	Depends on accurate isotope ratios, monitor-isotope quality, matrix behavior, and validated equations.
Helium collision / KED	Broadly attenuates many polyatomic ions through collisional energy loss.	Does not solve all elemental isobars or all doubly charged overlaps.

Strategy	Best suited for	Key limitation
Reactive cell gas	Uses ion-molecule chemistry to remove interference or shift analyte/interferent behavior.	Reaction chemistry can be analyte- and matrix-specific; may create new product ions if poorly controlled.
Tandem ICP-MS / mass-shift methods	Provides additional mass filtering before/after reaction chemistry.	Instrument-specific; method must be validated for the application.
Internal standardization	Compensates for many non-spectral changes in transport, ionization, transmission, and drift.	Does not by itself remove analyte-specific spectral overlaps.
Matrix matching	Reduces response differences between calibration standards and samples.	Can be difficult when sample composition varies widely.
Dilution	Reduces matrix loading and some matrix-derived interferences.	Also lowers analyte concentration and can increase relative impact of contamination.
Separation / sample preparation	Removes interfering components before measurement.	Adds preparation time and potential contamination or analyte-loss risk.

Where Interference Check Standards Fit

Interference control should be verified, not assumed. An interference check standard provides a defined challenge solution that can help evaluate whether potentially interfering elements or species affect determination of target analytes under the analytical conditions being used.

The composition, concentration, frequency, and acceptance criteria of an interference check must follow the applicable method or laboratory quality program. A general-purpose check solution should not be substituted for a method-specific requirement without technical justification.

CPI International offers ICP Interference Check Standards within its ICP Quality Control Standards category for ICP-MS and ICP-OES spectral-interference evaluation, method verification, instrument performance, and laboratory QC.

Common ICP-MS Interference Patterns

Observed pattern	What to investigate
Arsenic is biased high in a chloride-rich matrix	Consider 40Ar35Cl+ at m/z 75 and other matrix-dependent effects. Evaluate cell mode/reaction chemistry, matrix reduction, appropriate correction, and method-specific QC.
Chromium increases in a high-carbon matrix	Consider 40Ar12C+ at m/z 52. Compare alternative isotope behavior and evaluate collision/reaction-cell performance.

Observed pattern	What to investigate
Several analytes are suppressed and internal standards fall	A non-spectral matrix effect or sample-introduction/interface loading may be more likely than a single spectral overlap. Check dissolved solids, cones, nebulization, dilution, and matrix matching.
Only one isotope is biased while another agrees with QC	A mass-specific spectral interference is likely. Investigate isobaric/polyatomic overlap and correction mode.
Blank rises after a high sample	Suspect carryover or contamination before assuming a spectral interference. Extend rinse, inspect sample introduction, and repeat the blank.
Low-level analyte near a very intense adjacent mass is elevated	Evaluate abundance sensitivity, mass calibration/resolution, matrix concentration, and alternate isotope options.

Frequently Asked Questions

What causes ICP-MS interferences?

ICP-MS interferences arise when another species contributes signal at the analyte m/z or when the sample matrix changes sample transport, ionization, ion extraction, transmission, or detector response. Common sources include plasma argon, acids, water, matrix elements, molecular-ion formation, overlapping elemental isotopes, doubly charged ions, high dissolved solids, and carryover.

What are polyatomic interferences in ICP-MS?

Polyatomic interferences are molecular ions containing two or more atoms that have the same nominal mass-to-charge ratio as the analyte isotope. Examples can form from argon, oxygen, carbon, chlorine, sodium, sulfur, phosphorus, and other sample or plasma components.

What is the difference between an isobaric and a polyatomic interference?

An isobaric elemental interference is caused by an atomic isotope of another element at the same nominal m/z. A polyatomic interference is caused by a multi-atom ion at the analyte m/z. The distinction matters because correction strategies differ.

Does helium collision mode remove all ICP-MS interferences?

No. Helium collision with kinetic energy discrimination is broadly effective for many polyatomic ions, but it does not resolve every elemental isobar or every doubly charged overlap. Some problems require alternate isotopes, reactive gases, mathematical correction, higher-resolution or tandem-MS approaches, matrix separation, or another validated method.

Can an internal standard correct spectral interference?

Not generally. Internal standards are especially useful for non-spectral changes such as sample-introduction effects, matrix suppression/enhancement, ion transmission changes, and drift. An analyte-specific spectral overlap usually requires an interference-specific correction.

How can I tell whether an ICP-MS problem is a matrix effect?

Look for coordinated suppression or enhancement across multiple analytes/internal standards, dependence on dissolved-solids or acid content, changes as the sample is diluted, or progressive interface loading. Isotope-specific bias points more strongly toward a spectral interference.

Should I dilute a difficult sample?

Dilution can reduce matrix loading and some matrix-derived interferences, but it also reduces analyte concentration. Whether dilution is appropriate depends on reporting limits, method requirements, analyte concentration, contamination risk, and the instrument's validated operating range.

What is an ICP-MS interference check standard?

It is a defined solution used to evaluate the effect of potentially interfering species or high matrix-element concentrations on target analytes. The exact composition and acceptance criteria should match the applicable method or quality-control procedure.

Interference Control Starts with the Analytical Question

A high signal at an analyte mass is not proof that the analyte concentration is high. Reliable ICP-MS results require the laboratory to understand what else can contribute to that signal—and what can change the response before the ion reaches the detector.

Start by identifying the interference mechanism. Then select the isotope, correction mode, matrix-control strategy, internal standards, and QC materials appropriate to the method.

Technical References

- U.S. EPA — Method 200.8, Revision 5.4: Determination of Trace Elements in Waters and Wastes by ICP-MS
- Thermo Fisher Scientific — How to Improve Your ICP-MS Analysis, Part 2: Interferences
- Thermo Fisher Scientific — Technical Note 43427: ICP-MS detection limits and interference removal
- Agilent Technologies — Collision/reaction-cell approaches and reaction data for ICP-MS/MS
- Agilent Technologies — Comparing single and triple quadrupole ICP-MS
- Analytica Chimica Acta — Matrix effects in inductively coupled plasma mass spectrometry: A review

Method-specific requirements, correction equations, acceptance criteria, tuning limits, and QC frequencies should always be verified against the current applicable method, instrument documentation, and laboratory quality system before use.