# Internal Standards for ICP-MS: Selection, Purpose & Use

A practical guide to internal standard selection, addition, monitoring, and troubleshooting for ICP-MS elemental analysis.

**Quick answer:** An internal standard in ICP-MS is an element added at a consistent concentration to blanks, calibration standards, QC materials, and samples. Its signal is used to monitor and correct changes in response caused by instrument drift, sample introduction variation, and matrix effects. The internal standard should not be a target analyte or a meaningful native component of the sample, and it should behave similarly to the analytes it corrects.

### About the EPA Method Example in This Guide

The internal-standard 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 the purpose, selection, addition, concentration and monitoring of internal standards. Its repeated use is illustrative and does not mean that the guidance, internal-standard solutions or CPI products discussed are limited to EPA Method 200.8 or to the analysis of water and waste samples.

Internal-standard elements, concentrations, analyte assignments, addition procedures and response criteria can vary among regulatory methods, industry procedures, instrument configurations and laboratory-developed methods. Laboratories should confirm the applicable requirements using their analytical method, instrument instructions, validated SOPs and quality system.

## Why Internal Standards Matter in ICP-MS

ICP-MS is widely used for trace and multi-element analysis because it can measure many elements at low concentrations. That sensitivity also means the measurement can be affected by changes that occur during sample introduction, ion transmission, and detection.

Internal standards provide a way to monitor those changes while samples are being analyzed. Rather than relying only on the absolute signal of the analyte, the instrument can compare analyte response to the response of an internal standard added at a known, consistent level.

EPA Method 200.8 defines an internal standard as a pure analyte added to a sample, extract, or standard solution in a known amount and used to measure relative responses of other method analytes; the method also states that the internal standard must not be a sample component. EPA Method 200.8 further explains that instrumental drift and matrix-related suppression or enhancement must be corrected through internal standards.

In practical laboratory terms, internal standards help answer one essential question: did the measured analyte response change because the sample concentration changed, or because the instrument/sample-introduction system changed?

## What is an Internal Standard in ICP-MS?

An ICP-MS internal standard is an element or isotope added to every measured solution at the same effective concentration. The internal standard is measured along with the target analytes and used to correct analyte signals for response changes that occur during analysis.

Internal standards are commonly used in:

- Calibration blanks

- Calibration standards
- Initial and continuing calibration verification standards
- Quality-control samples
- Method blanks and laboratory reagent blanks, when applicable
- Unknown samples
- Spikes, duplicates, and other method-specific QC materials

The key point is consistency. The internal standard must be added to all relevant solutions in the same manner so that the correction reflects analytical variation rather than preparation inconsistency.

## Why Are Internal Standards Used?

Internal standards are used to compensate for changes in instrument response that would otherwise bias the measured analyte concentration. They are especially useful in ICP-MS because matrix effects and signal drift can occur even when calibration standards were prepared correctly.

### Internal standards can help compensate for:

- Instrument drift during an analytical sequence
- Changes in sample introduction efficiency
- Nebulizer or spray-chamber variation
- Matrix-induced signal suppression or enhancement
- Physical differences between samples and standards
- Short-term signal fluctuation
- Certain mass-dependent response changes

### Internal standards do not solve every problem

Internal standard correction is not a substitute for method control. It cannot automatically correct spectral overlap, poor sample preparation, contamination, incorrect calibration, inappropriate dilution, or an internal standard that is itself interfered with.

Internal standardization should therefore be combined with appropriate calibration, blanks, quality-control checks, interference evaluation, and method-specific acceptance criteria.

## What Internal Standards Correct, and What They Do Not

| Issue | Internal standard can help? | Notes |
|---|---|---|
| Instrument drift | Yes | Useful when the internal standard experiences similar drift to the analyte. |
| Sample transport differences | Often | Can help compensate for nebulization and transport variation. |
| Matrix suppression/enhancement | Often | Correction depends on internal standard behaving similarly to the analyte. |
| Polyatomic or isobaric interference | No / limited | Requires isotope selection, interference correction, collision/reaction cell methods, or other controls. |
| Incorrect standard preparation | No | Internal standardization cannot repair an incorrectly prepared calibration standard. |
| Contamination | No | Use blanks, clean preparation, reagent control, and appropriate lab practices. |
| Internal standard present in sample | Problematic | Can cause correction error if native concentration is significant. |

# How Are Internal Standards Selected?

An internal standard should behave as much like the analyte as practical while remaining distinguishable from the analyte and absent from the sample at meaningful levels.

No single internal standard is ideal for every analyte or matrix. Multi-element ICP-MS methods often use several internal standards distributed across the mass range so each analyte can be corrected using a suitable reference element.

## Key selection criteria

- The internal standard should not be a target analyte in the method.
- It should not be present in the sample at a concentration that materially changes the added internal-standard signal.
- It should have similar mass and/or ionization behavior to the analyte it corrects.
- It should remain soluble and chemically compatible with the calibration and sample matrix.
- It should be free from significant spectral or polyatomic interference under the operating conditions.
- It should not create interferences on target analytes.
- It should produce a stable, measurable signal at the selected concentration.
- It should meet the requirements of the analytical method and instrument configuration.

Agilent ICP-MS technical guidance describes internal-standard selection using similar behavior, mass number and/or ionization potential; Thermo Fisher's ICP-MS data-analysis guidance similarly notes that internal standards should be absent from the sample, have similar mass and ionization potential, and behave similarly in solution and in the plasma.

# Common ICP-MS Internal Standard Elements

Common ICP-MS internal standard elements include scandium, yttrium, rhodium, indium, terbium, holmium, lutetium, bismuth, lithium-6, gallium, germanium, and others depending on the method and instrument.

EPA Method 200.8 gives a general application procedure using scandium, yttrium, indium, terbium, and bismuth. The method also states that, for full mass range scans, a minimum of three internal standards must be used and that internal standards must be present in all samples, standards, and blanks at identical levels.

| Element | Approx. mass | Typical role | Selection caution |
|---|---|---|---|
| Scandium | 45 | Low-mass/mid-mass correction in some methods | May not match high-mass analytes well. |
| Yttrium | 89 | Common mid-mass internal standard | Can be present in some environmental samples. |
| Rhodium | 103 | Common mid-mass internal standard | Verify interference and method compatibility. |
| Indium | 115 | Common mid-mass internal standard | Useful for many elements; verify sample absence. |
| Terbium | 159 | Mid/high-mass internal standard | Confirm instrument sensitivity and interference status. |
| Holmium | 165 | Mid/high-mass internal standard | Method and instrument dependent. |
| Lutetium | 175 | High-mass internal standard | Method and instrument dependent. |
| Bismuth | 209 | High-mass internal standard | Often used near Pb and other high-mass analytes. |

Note: This table is a practical orientation tool, not a universal assignment table. Always follow the method, instrument configuration, sample matrix, and laboratory validation data. Some methods or instruments may use additional internal standards such as enriched lithium-6; verify applicability before use.

# How Are Internal Standards Added?

Internal standards can be added in more than one way. The correct approach depends on the method, instrument setup, and laboratory procedure.

### 1. Direct addition

The internal standard solution is added directly to each blank, calibration standard, QC material, and sample. This approach requires consistent volumetric addition and enough mixing to ensure homogeneity.

### 2. Online addition by peristaltic pump

The internal standard solution is introduced through a separate pump channel and mixed with the sample stream before nebulization. This can improve consistency during routine sequences, but tubing dimensions, uptake rate, mixing volume, and stabilization time become important.

EPA Method 200.8 describes both direct addition and online addition by a second peristaltic-pump channel and mixing coil.

### What matters either way

- The internal standard must be added to all measured solutions consistently.
- The final internal-standard concentration should be appropriate for the instrument response.
- The internal-standard solution matrix should be compatible with samples and standards.
- The internal-standard signal should be stable before data collection begins.
- The addition approach should not create a meaningful dilution difference between standards and samples.

## Internal Standard Concentration

There is no universal concentration for every ICP-MS method. The concentration must be high enough to provide good measurement precision but low enough to avoid contamination, detector issues, or interference problems.

EPA Method 200.8 recommends 20–200 µg/L of each internal standard, depending on instrument sensitivity. Other methods, instruments, and applications may require different concentrations.

For online addition, the internal-standard stock solution may need to be more concentrated than the effective concentration reaching the nebulizer because the internal-standard pump channel may deliver a smaller flow than the sample channel.

## How Internal Standard Correction Works

In simplified terms, ICP-MS software monitors the internal-standard response during analysis and compares it with the response observed during calibration. If the internal-standard signal changes, the software applies a correction to associated analytes according to the method and instrument settings.

A simplified correction concept is:

Corrected analyte response = measured analyte response adjusted by the relative internal-standard response

The correction assumes that the analyte and assigned internal standard are affected similarly. That assumption is why internal-standard selection matters.

## How to Assign Internal Standards to Analytes

For multi-element ICP-MS methods, internal standards are often assigned across the mass range. A low-mass analyte should not automatically be corrected by a high-mass internal standard simply because the internal standard signal is strong.

A practical assignment process:

1. Start with the applicable analytical method and any required internal-standard list.
2. Group analytes by approximate mass range and behavior.

3. Review potential spectral, polyatomic, and sample-matrix interferences for each internal standard.
4. Evaluate whether the internal standard is naturally present in the sample type.
5. Confirm the internal-standard signal is stable and sufficiently intense.
6. Validate the assignment using QC recovery, drift checks, matrix spikes, and representative samples.
7. Document assignments in the method or instrument data-processing settings.

## Internal Standard Selection Checklist

| Selection question | Why it matters |
|---|---|
| Is it listed or allowed by the method? | Method requirements take precedence over generic selection rules. |
| Is it absent from the sample? | Native internal-standard element in the sample can bias correction. |
| Is the mass reasonably close to the analyte? | Mass-dependent drift and transmission effects may differ across mass range. |
| Is ionization behavior similar? | Similar ionization behavior helps the internal standard track analyte response. |
| Is the isotope free from interference? | An interfered internal-standard signal produces incorrect correction. |
| Is the signal stable and precise? | Weak or unstable internal-standard signal can increase noise. |
| Is the solution chemically compatible? | Matrix incompatibility can cause instability or precipitation. |
| Does it interfere with target analytes? | The internal standard should not create a new analytical problem. |

## Monitoring Internal Standard Responses

Internal-standard response should be monitored throughout the analytical sequence, not only during initial setup. EPA Method 200.8 expects analysts to monitor internal standard responses throughout the sample set and to monitor ratios of internal-standard responses against each other to detect potential problems.

A sudden or progressive change in internal-standard response can indicate:

- Nebulizer blockage or instability
- Pump tubing wear or uptake inconsistency
- Matrix deposition on cones
- Instrument drift
- Incorrect internal-standard addition
- Air bubbles or mixing problems
- High dissolved solids or matrix suppression
- Memory effects or carryover
- Interference on the internal-standard isotope

The corrective action depends on the method and laboratory SOP. Analysts should avoid treating internal-standard correction as a black box; the internal-standard trend is diagnostic information.

## Troubleshooting Internal Standard Problems

### Internal-standard response is low

- Check internal-standard solution concentration and expiration/stability.
- Confirm the internal standard is being added to all solutions.
- Inspect pump tubing, mixing tee/coil, fittings, and uptake lines.
- Check nebulizer, spray chamber, cones, and sample-introduction components.
- Evaluate high dissolved solids or matrix suppression.
- Verify instrument tuning and mass calibration.

### Internal-standard response is high

- Check for carryover from a previous high concentration internal-standard solution.
- Confirm the internal-standard solution was diluted correctly.
- Verify the internal-standard element is not present in the sample or reagent matrix.
- Review data-processing settings and isotope assignments.

### Internal-standard response drifts during the sequence

- Inspect sample-introduction stability.
- Check for cone deposition or matrix buildup.
- Evaluate whether rinse time is sufficient.
- Confirm plasma and interface conditions are stable.
- Review whether the sample matrix differs substantially from calibration standards.

### Internal-standard recovery is acceptable but analyte recovery fails

This can happen. Internal standardization may compensate for some signal changes, but it does not eliminate all interferences or matrix effects. Investigate analyte-specific interference, spike recovery, calibration range, sample preparation, dilution, and method-specific QC.

## Internal Standards vs. Other ICP-MS Standards

| Material | Primary purpose | Not the same as |
|---|---|---|
| Internal standard solution | Corrects or monitors response changes during analysis | Calibration standard |
| Calibration standard | Establishes concentration-response relationship | Internal standard |
| ICV / QCS | Verifies initial calibration or method/instrument performance | Internal standard |
| CCV | Checks calibration during a run | Internal standard |
| Tuning solution | Evaluates setup, mass calibration, resolution, sensitivity, or stability | Internal standard |
| Interference check solution | Evaluates potential interference effects | Internal standard |

## When Should a Laboratory Use a Custom Internal Standard Solution?

A custom internal standard solution can be useful when a laboratory routinely runs the same ICP-MS method and requires a specific combination of internal standard elements, concentration, matrix, and volume.

Custom formulation may be appropriate when:

- The method uses a defined set of internal standards repeatedly.
- The laboratory wants fewer preparation steps.
- The same internal-standard mixture is used across routine sequences.
- The required matrix differs from a catalog formulation.
- The lab wants to reduce dilution or transcription errors.
- Inventory volume needs are predictable.

A custom solution should still be evaluated for compatibility, stability, and method suitability. The formulation should be based on actual analytical requirements, not convenience alone.

## How to Specify an ICP-MS Internal Standard Solution

Before requesting or preparing an internal-standard solution, define the analytical requirement clearly.

1. Analytical method or application
2. Target analytes
3. Required internal-standard elements
4. Desired concentration of each internal standard
5. Final matrix and acid concentration
6. Whether the solution is used for direct addition or online addition
7. Required volume and packaging
8. Any regulatory or quality-system requirements
9. Instrument platform and sample matrix, when relevant

Providing this information allows the formulation to be evaluated against the method, expected sample matrix, and laboratory workflow.

## Example of Internal Standard Requirements

EPA Method 200.8 provides a method-specific example. Important EPA Method 200.8 points include:

- The method uses ICP-MS for trace elements in waters and wastes.
- It identifies internal standards as a correction tool for instrumental drift and matrix-related suppression or enhancement.
- It describes the use of scandium, yttrium, indium, terbium, and bismuth for general application.
- It requires internal standards to be present in samples, standards, and blanks at identical levels.
- It describes either direct addition or peristaltic-pump addition using a second channel and mixing coil.
- It recommends an internal standard concentration range of 20–200 µg/L, depending on instrument sensitivity.
- It expects analysts to monitor internal standard responses throughout the sample set.

Because these are method-specific details, they should not be generalized to unrelated ICP-MS methods without confirming the applicable procedure.

## Internal Standard Selection Starts with the Method

Internal standards are one of the most important tools for reliable ICP-MS quantitation, but they must be selected and used correctly.

The best internal standard is not simply the element with the strongest signal. It is the element or combination of elements that meets the method requirements, behaves appropriately relative to the analytes, avoids significant interferences, remains compatible with the matrix, and produces stable correction across the analytical sequence.

For routine ICP-MS methods, a carefully selected internal standard solution can support more consistent calibration, QC, and sample analysis.

## Frequently Asked Questions

### What is an internal standard in ICP-MS?

An internal standard is an element or isotope added at a controlled concentration to blanks, calibration standards, QC materials, and samples. Its measured response is used to monitor and correct changes in analyte response caused by drift, sample introduction, or matrix effects.

### Why are internal standards used in ICP-MS?

They help compensate for instrument drift and matrix-related signal suppression or enhancement. EPA Method 200.8 specifically states that instrumental drift and matrix-related response changes must be corrected through internal standards.

### How are internal standards selected?

Internal standards should behave similarly to the analytes they correct, be absent from the sample at meaningful levels, avoid interferences, remain chemically compatible, and meet method-specific requirements.

### What are common ICP-MS internal standards?

Common examples include Sc, Y, Rh, In, Tb, Ho, Lu, Bi, Li-6, Ga, and Ge, depending on the method and instrument. EPA Method 200.8 describes general use of Sc, Y, In, Tb, and Bi.

### Does every ICP-MS method use the same internal standards?

No. Internal-standard choice depends on the method, analytes, mass range, sample matrix, instrument configuration, and interference profile.

### Should internal standards be added to calibration standards and samples?

Yes, when internal standardization is used, they should be present in the calibration standards, blanks, QC materials, and samples consistently. EPA Method 200.8 requires internal standards to be present in samples, standards, and blanks at identical levels.

### Can an analyte also be used as an internal standard?

Generally no. The internal standard should not be a sample component or target analyte. If it is naturally present in the sample at meaningful levels, correction errors can occur.

### Is an internal standard solution the same as a tuning solution?

No. A tuning solution evaluates instrument setup and performance. An internal standard solution is used during analysis to monitor and correct response changes.

## CPI ICP-MS Internal Standard Support

CPI International supplies analytical reference materials and custom inorganic standards for laboratories performing ICP-MS and other elemental analysis workflows.

For ICP-MS workflows, CPI can support laboratories with:

- Single Element ICP Standards
- ICP Calibration Standards
- ICP Quality Control Standards
- ICP Tuning and Setup Solutions
- Custom Inorganic Standards

For laboratories repeatedly preparing the same internal-standard mixture, CPI custom inorganic standards allow the lab to specify analytes, concentrations, matrix, volume, and other formulation requirements. This can help reduce routine preparation steps while aligning the solution with the laboratory's analytical method.

### Standardize Your Standards

## Sources and Verification Notes

Note: Method-specific requirements should always be verified against the current official method and the laboratory's approved SOP.


• U.S. EPA Method 200.8: Determination of Trace Elements in Waters and Wastes by Inductively Coupled Plasma-Mass Spectrometry, Revision 5.4: https://www.epa.gov/esam/epa-method-2008-determination-trace-elements-waters-and-wastes-inductively-coupled-plasma-mass

• EPA Method 200.8 PDF: https://www.epa.gov/sites/default/files/2015-06/documents/epa-200.8.pdf

• Agilent ICP-MS Help: Internal Standard Method and Standard Addition Method: https://icp-ms.help.agilent.com/en/HowTo/Help/Reference/Internal_Standard_Method_and_Standard_Addition_Method.htm

• Thermo Fisher Scientific: ICP-MS Data Analysis and Calibration Strategies: https://www.thermofisher.com/lc/en/home/industrial/spectroscopy-elemental-isotope-analysis/spectroscopy-elemental-isotope-analysis-learning-center/trace-elemental-analysis-tea-information/inductively-coupled-plasma-mass-spectrometry-icp-ms-information/icp-ms-data-analysis.html


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