

SmartNotes

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Single quadrupole ICP-MS instruments, such as the Thermo Scientific™ iCAP™ RQ ICP-MS, are the perfect choice for laboratories testing for trace elements in routine sample matrices, from water analysis and food testing to elemental impurities analysis in the pharmaceutical industry and industrial applications.

Single quadrupole based instruments use Kinetic Energy Discrimination (KED), a generic interference removal mechanism that uses helium as a collision gas, to remove polyatomic interferences, which are generally of most concern in ICP-MS. This is in many cases the best way to analyze transition metals such as chromium, copper, zinc or nickel, or heavy metals such as cadmium, mercury, lead and uranium. Applying KED, with helium as a collision gas, for all analytes in a single mode of analysis, results in single quadrupole systems being unmatched in simplicity of method set up and in sample turnover times. This note will highlight key technical solutions to enable robust and highly sensitive analysis of trace elements using single quadrupole ICP-MS, and provide information on potential differences and advantages when considering triple quadrupole ICP-MS.

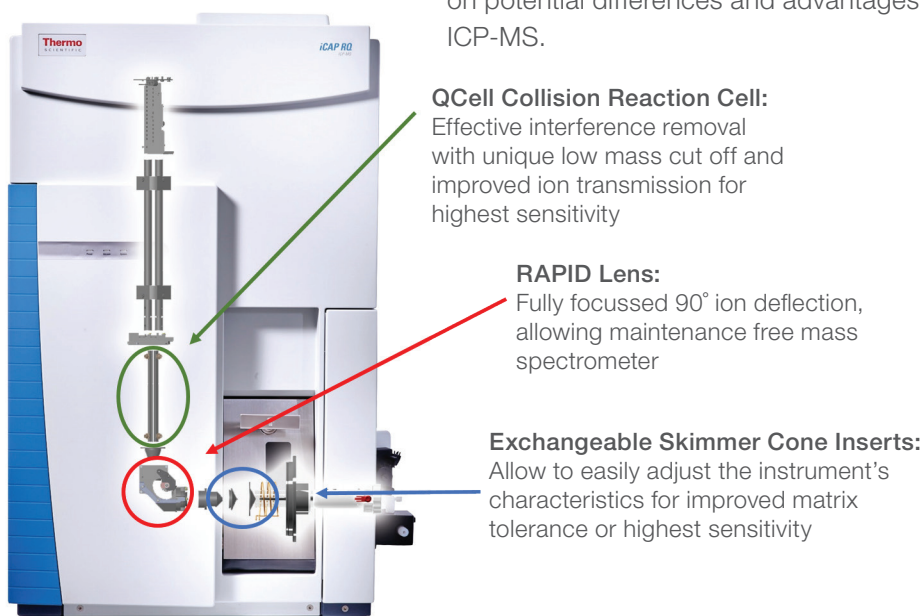


Figure 1. Schematic of the iCAP RQ ICP-MS and its key components for robust and reliable multi-elemental analysis.

What are the limiting factors for matrix content in ICP-MS?

Although ICP-MS and ICP-OES are very similar in design of the sample introduction system and the plasma source, it is well known that in contrast to ICP-OES, ICP-MS is far less tolerant to sample matrix load, commonly expressed as total dissolved solids (TDS). Whereas an ICP-OES can easily tolerate up to 4% of TDS without changes to the sample introduction system, the upper limit for ICP-MS, without considering special solutions such as gas dilution, is typically 0.3% of TDS. The reason for this is the fact that ions are generated in the plasma at atmospheric pressure and need to be extracted into the high vacuum of the mass analyzer. This is accomplished in the so-called interface region, comprising of two narrow apertures (sample and skimmer cones). Very high amounts of salts can deposit on the surface of the sample and skimmer cones and reduce ion transmission significantly, leading to instrument downtime, as maintenance (i.e. cleaning of the cones) becomes required. Different design of the cones (especially the skimmer cone) may influence the instrument's characteristics and significantly affect matrix tolerance. The iCAP RQ ICP-MS, with exchangeable skimmer cone inserts of variable channel length, allow easy customization of the instrument's performance characteristics. The standard insert used on the iCAP RQ ICP-MS allows analysis of samples with a broad range of dissolved solids and represents a generic solution for all sample matrices. Through its versatile working range, it is not required to exchange the skimmer cone insert during a run with mixed sample matrices.

Other inserts allow to increase the sensitivity and obtain lowest detection limits, or to increase robustness of the system in order to analyze most challenging sample matrices, such as waste water or soil digests. Table 1 gives an overview on the available options.

Table 1. Different Skimmer Cone Inserts and options available for the iCAP RQ ICP-MS and iCAP TQ ICP-MS with typical application areas.

TDS in sample	Skimmer cone insert	Comment
Below 0.1%	High Sensitivity	Use for pure solutions
Up to 0.3%	High Matrix	Universal solution, applicable for most analysis
Up to 0.5%	Robust	High TDS samples; Can also be used for extension of calibration ranges up to 5000ppm
Higher than 0.5% and up to 3-4%	AGD	Direct analysis of e.g. brackish waters; Requires additional hardware
Up to 25%	Combination of AGD and in-line dilution	Requires additional hardware

Which is better, gas or liquid dilution?

For analysis using ICP-MS, some samples containing higher amounts of TDS need to be diluted to avoid the aforementioned adverse effects on the interface region. In principle, there are multiple ways to achieve this:

- Gas dilution using argon gas is a way to dilute a sample before it enters the plasma. This approach is often perceived as simple and cost effective, as the samples can be loaded directly onto the autosampler. However, through the process of dilution, the instrument's performance is significantly reduced and some elements with elevated 1st ionization potentials (such as As, Se, Cd or also Zn) may suffer from lower recoveries. As the undiluted sample is in contact with different parts of the sample introduction system, cross contamination may become an issue and potentially varying viscosity of different samples may bias results. Normally, a single fixed dilution factor is applied for all samples, regardless whether a lower or higher dilution factor would be beneficial.
- Liquid dilution allows more flexibility, as the dilution factor can be varied while preparing the samples. Although diluents add cost per analysis, this approach is often superior as the ICP-MS system can be run under optimum conditions and cross contamination can be reduced.

Using an autosampler capable of automatic and intelligent in-line dilution, labor intensive steps like preparation of calibration standards as well as manual re-runs of samples exceeding the internal standard or QC recovery targets, can be performed automatically by the system. The automatic dilution process can be fully controlled by Qtegra ISDS Software, leaving operators more time for other tasks and allowing for complete traceability of all dilution steps. In contrast to gas dilution, the set up and maintenance of the sample introduction system is significantly easier as valves can be fully integrated in close proximity of the system.

What is better, a linear design with a photon stop or 90° offset of the ion beam?

It is important to remove photons and neutral atoms/molecules from the ion beam as they could cause unwanted signals in the detection system. Generally, 90° deflection removes photons and neutrals more efficiently and can reduce the instrument's footprint considerably in comparison to a linear design with photon stops or off axis lenses. Either way, it is clear that any device bending the direction of the ion beam should do this at a point where the ion beam dimension is minimal to ensure effective deflection. In addition, the active lens surfaces should not be exposed to the unwanted material, as this would contaminate over time and significantly reduce performance or require additional maintenance, especially when located in the high vacuum region of the analyzer. If a fit for purpose 90° ion deflection system is used, such as the RAPID lens on the iCAP RQ ICP-MS and iCAP TQ ICP-MS, ICP-MS features an essentially maintenance free mass spectrometer.

How are interferences removed on a single quadrupole ICP-MS?

Kinetic energy discrimination is a generic approach to eliminate interferences in ICP-MS. In KED, the collision/reaction cell (CRC) is flushed with helium at a flow rate of about 5 mL·min⁻¹. This in turn will lead to collisions between all ions travelling through the CRC and helium atoms. Due to its inert nature, there will be no chemical reactions or charge transfers resulting from these collisions, but all ions will be slowed down.

Since polyatomic interferences consist of at least two or more atoms, they have a larger cross sectional area in comparison to the analyte ion and will undergo more collisions. Therefore, they will lose more kinetic energy and will not be able to exit of the CRC and enter the analyzing quadrupole and subsequently the detector.

Although this leads to a slight loss in sensitivity as compared to standard mode, the signal to noise ratio is often improved dramatically. Figure 1 shows how kinetic energy discrimination will remove chlorine based interference from ⁷⁵As⁺, the most severe interference for this element.

On the iCAP RQ ICP-MS, interference removal using KED is complemented by a second active mechanism. Low mass cut off is a unique characteristic of flatapoles, used in the QCell CRC, to remove lower mass precursor ions from the ion beam, and inhibiting formation of new interference. Not only are there analyte ions and polyatomic interferences traveling through the mass spectrometer, there are also numerous precursor ions (i.e. ⁴⁰Ar⁺ or ⁴⁰Ca⁺, ³⁵Cl⁺) that can potentially form more polyatomic interferences in the CRC. The flatapole design of the QCell allows the use of a dynamically adjusted low mass cut off feature, automatically set for every analyte and not requiring interaction or optimization by the operator.



Quadrupole set to filter out exact mass of target analyte

QCell in collision mode with pure He uses energy discrimination

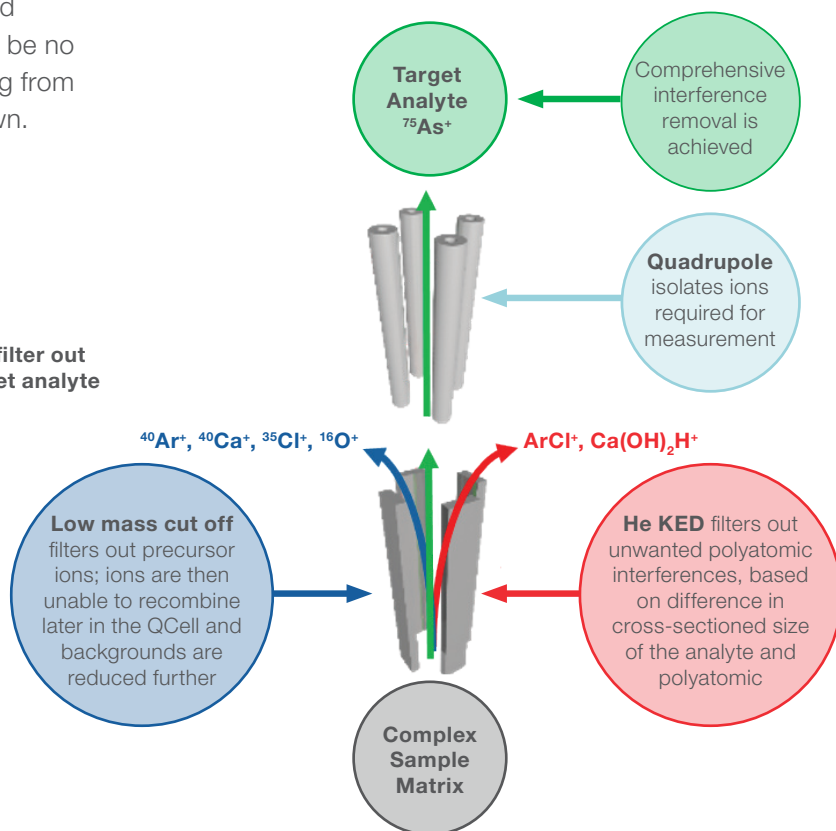


Figure 2. Interference removal using kinetic energy discrimination (KED) and low mass cut-off on an iCAP RQ ICP-MS.

With low mass cut off, the lowest instrumental detection limits (IDL) and blank equivalent concentrations (BEC) are consistently achieved. Since low mass cut off is based on the unique characteristic of flatapoles (more exactly their well-defined stability regions for a given m/z), it is not available on higher multipoles used in collision/reaction cell systems. Figure 3 shows a picture of the QCell and a schematic illustrating the physical background of low mass cut off feature.

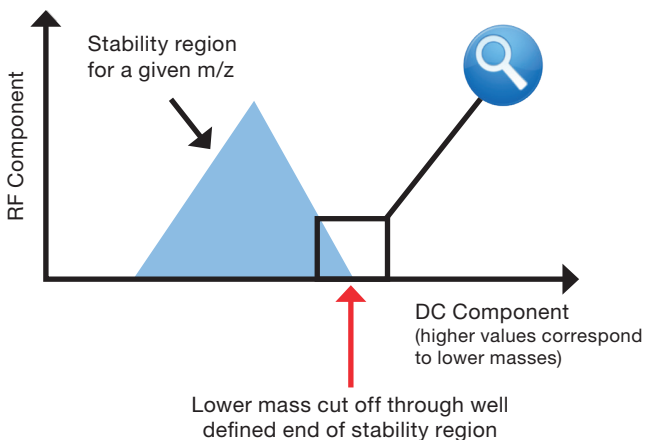
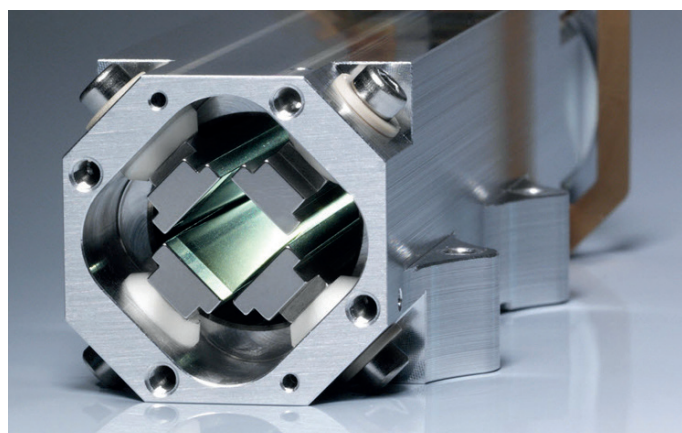


Figure 3. Illustration of the Low Mass Cut Off feature, unique to flatapole based CRC systems.

Why should I buy a single quadrupole ICP-MS now? Aren't triple quads going to replace them anyway?

It is true that triple quadrupole based ICP-MS instruments, such as the Thermo Scientific™ iCAP™ TQ ICP-MS, have made a great step forward and are being adopted more and more in routine analysis laboratories, due to the significant improvement in ease of use and method set up. Modern software tools such as the Reaction Finder method development assistant included in the Thermo Scientific™ Qtegra™ Intelligent Scientific Data Solution (ISDS) Software allow even inexperienced users to apply reactive gases and different analysis modes to fully leverage the potential of these instruments in removing interferences and improving detection limits.

What is the difference between a single and a triple quadrupole ICP-MS?

Triple quadrupole ICP-MS systems feature an additional quadrupole acting as an active mass filter before the CRC. This mass filter pre-selects ions of a specific mass to charge ratio (i.e. an analyte with interferences having the same nominal mass) before they enter the CRC. To be able to perform mass separation, it is important that the quadrupole mass filter is situated axially along the ion beam (see Figure 4). Quadrupoles can be used as ion deflection devices if they are mounted perpendicular to the ion beam, but this does not allow mass filtration and therefore does not enable triple quadrupole operation.

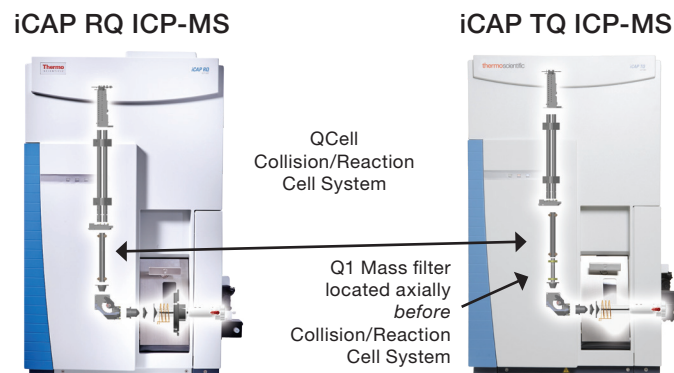


Figure 4. Positioning of a Q1 mass filter in a triple quadrupole ICP-MS system.

Triple quadrupole ICP-MS allows the use of reactive gases effectively and hence leverages chemical interference removal through dedicated ion molecule reactions in the gas phase. More information on triple quadrupole ICP-MS and interference removal can be found in dedicated literature.

How does triple quadrupole ICP-MS resolve interferences?

In contrast to triple quadrupole systems commonly used for LC-MS or GC-MS applications, in ICP-MS the analyte of interest cannot be broken down any further (to elucidate structural information). Full decomposition has already been accomplished while going through the inductively coupled plasma ion source. In triple quadrupole ICP-MS, interferences can be removed through the addition of reactive gases that react either with the analyte or the interference to form a new product ion at a different mass from the original mass to charge ratio:

- $^{75}\text{As}^+$ is converted to $^{75}\text{As}^{16}\text{O}^+$ using O_2 , whereas interfering $^{40}\text{Ar}^{35}\text{Cl}$ does not react.
- $^{95}\text{Mo}^{16}\text{O}^+$ interfering on $^{111}\text{Cd}^+$ is forming $^{95}\text{Mo}^{16}\text{O}_2^+$ with O_2 whereas $^{111}\text{Cd}^+$ does not react).

In both cases, the first quadrupole removes all ions of lower and higher mass, which could potentially create interfering reaction products or remain as unresolved interferences at the mass to charge ratio of the product ion.

However, the inherent additional complexity of triple quadrupole ICP-MS (in comparison to single quadrupole ICP-MS) is a potential barrier when adopting the technology. The Reaction Finder method development assistant greatly simplifies the process by pre-selecting the right combination of reactive gas, scan mode and product ion (where applicable) based on the user's element selection, without restricting or limiting functionality for experienced or expert users.

Can I use reactive gases on my single quadrupole instrument?

On a single quadrupole instrument, all ions will pass through the CRC filled with a reactive gas. Therefore, a number of different reaction products may be formed for a given sample composition, which will result in the formation of many new interferences. With exception of hydrogen (which can induce effective charge neutralizations to remove e.g. $^{40}\text{Ar}^{2+}$ or $^{40}\text{Ar}^{16}\text{O}^+$), the use of reactive gases is only recommended on triple quadrupole instruments such as the iCAP TQ ICP-MS. However, on a single quadrupole system, the use of hydrogen is an effective means to significantly reduce the detection limits for challenging isotopes such as ^{80}Se and ^{56}Fe , respectively.

Table 2 highlights the risk of potentially observed false positive results for arsenic and selenium when analyzing a solution containing $100 \text{ ng}\cdot\text{mL}^{-1}$ of neodymium, gadolinium, dysprosium, molybdenum and zirconium. In addition, solutions containing $50 \text{ }\mu\text{g}\cdot\text{L}^{-1}$ Ca and Fe, which can both be present in environmental samples at these levels were tested for their impact on the analytes.

Table 2. Results for the analysis of arsenic and selenium using reactive gases in single and triple quadrupole modes.

Analyte	Gas	Mode	BEC in Matrix [$\mu\text{g}\cdot\text{L}^{-1}$]	$1 \text{ }\mu\text{g}\cdot\text{L}^{-1}$ Spike Recovery [%] in Matrix	BEC in 50 ppm Ca [$\mu\text{g}\cdot\text{L}^{-1}$]	BEC in 50 ppm Fe [$\mu\text{g}\cdot\text{L}^{-1}$]
^{75}As	O_2	SQ ($^{75}\text{As}^{16}\text{O}^+$)	0.08	93 ± 2	0.01	3.00
		TQ ($^{75}\text{As}^{16}\text{O}^+$)	0.004	101 ± 1	0.002	0.04
^{78}Se	O_2	SQ ($^{78}\text{Se}^{16}\text{O}^+$)	26.6	-27 ± 1	0.33	0.66
		TQ ($^{78}\text{Se}^{16}\text{O}^+$)	0.003	103 ± 3	0.01	0.02
^{80}Se	O_2	SQ ($^{80}\text{Se}^{16}\text{O}^+$)	22.0	17 ± 2	0.01	0.67
		TQ ($^{80}\text{Se}^{16}\text{O}^+$)	0.005	102 ± 2	0.002	0.02

As can be seen, some components of the matrix induce false positive signals and often, interferences can be aggravated in single quadrupole modes when using non-KED analysis conditions and reactive gases in the CRC. Whilst the analysis of arsenic and selenium using a mass shift reaction with oxygen may be a viable option for a triple quadrupole based system, there are several limitations on a single quad instrument:

- Elements of higher mass than the analyte may potentially cause interferences at the intended product ion mass of the reaction: Significantly higher background signals are observed due to unresolved $^{91}\text{Zr}^+$ (interfering with $^{75}\text{As}^{16}\text{O}^+$) and $^{94, 96}\text{Mo}^+$ (interfering with $^{78, 80}\text{Se}^{16}\text{O}^+$), rendering Se quantitation practically useless.
- Elements with lower mass may react with the cell gas as well and create new interferences with same m/z charge as the analyte: The presence of Fe causes a false positive signal on m/z 91, 94 and 96 (e.g. $^{56}\text{Fe}(\text{OH})_2\text{H}^+$).

Although features such as a bandpass filter, applied as an extension to low mass cut off, could potentially help to reduce the impact of unwanted ions from other components in the sample, only a true mass filter situated in front of the CRC, as in triple quadrupole ICP-MS, will be able to fully overcome these and assure consistent and reliable quantification.

Which collision/reaction gases do I need to run my system effectively?

Choosing which collision/reaction gas is required, or beneficial, highly depends on the objectives of the analysis. Most routine laboratories working with single quadrupole ICP-MS will be able to remove the majority of interferences using helium and KED. If elements such as Fe or Se are of interest, or could be in the future, hydrogen is a good addition to the CRC as it allows removal of intense polyatomic interferences on the most abundant isotopes of these elements. As shown by the results in Table 2, the use of reactive gases is not generally recommended on single quadrupole ICP-MS instruments. However, for some analytes, specific reactions can be beneficial in case the sample matrix is known.

If triple quadrupole ICP-MS is a potential solution, helium and oxygen are the most important gases. Oxygen induces a wide range of reactions facilitating the detection of critical elements such as As or Se regardless of other components in the matrix thanks to the additional mass filtration capability. For research driven laboratories, or if special analytes (e.g. rare earth elements) are of interest, all gases, especially ammonia, should be available.

Table 3 gives an overview on the different gases and their importance for either single or triple quadrupole instruments.

Table 3. Overview on reactive gases and their importance in single and triple quadrupole ICP-MS.

Gas	#	Single Quad ICP-MS	#	Triple Quad ICP-MS
		Reason		Reason
He	1	KED as generic interference removal tool	1	KED as generic interference removal tool
H ₂	2	May help to significantly improve DLs for Fe, Se due to charge neutralization of affecting polyatomics (e.g. ⁴⁰ Ar ₂ ⁺ , ⁴⁰ Ar ¹⁶ O ⁺)	4	Low number of product ions, low yield. For elements where improvement is seen with SQ, there are more effective reactions with O ₂ on a TQ system (e.g. As, Se etc.)
O ₂	3	Useful for some analytes (e.g. S, P), but high risk of side reactions	2	O ₂ forms a variety of product ions that can significantly improve interference removal and DLs
NH ₃	4	Not recommended due to uncontrollable side reactions	3	Specific reactions for some analytes (e.g. Ti, rare earth elements)

What else do I need to consider before starting analysis of trace elements?

Since ICP-MS is a very sensitive technique, it is imperative to carefully access the laboratory conditions and potential contamination coming from sample vessels, flasks and reagents (e.g. acids and ultrapure water for preparation of standards and samples). For ICP-MS analysis, the highest purity grade of acid is recommended (i.e. Fisher Scientific™ OPTIMA™ acids). It is recommended to test new batches of vials for potential sources of contamination. If samples are digested using a microwave system, a digestion blank must be included in each sample batch to screen for potential contaminations introduced in the digestion process. This can greatly simplify troubleshooting in case false positive results are observed. For the best system performance, the laboratory infrastructure needs to meet pre-installation requirements for utilities, ventilation, gas purity and supply requirements for gases used in the CRC. To consistently achieve sub ng·mL⁻¹ detection limits, dust covers for autosamplers and a laminar flow hood for sample preparation are recommended.

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