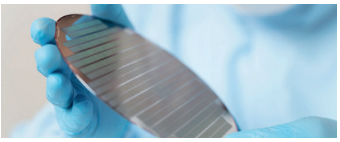
Agilent ICP-MS Journal

November 2022, Issue 90



Novel Sample Types, New Applications, and the Latest Revision of ICP-MS Software

Issue 90 of the Agilent ICP-MS Journal includes a review of a recent Agilent webinar on the alternative protein industry and the requirements for analytical methods to support it.

We also introduce the latest revision of Agilent ICP-MS MassHunter software, version 5.2, with a summary of new features, compatibility, and some of the applications enabled by the new revision.

Single nanoparticle analysis now allows an unlimited number of analytes to be measured in nanoparticles in each sample. Compound independent calibration for chromatography now supports multi-injection calibrations. Finally, a new function to normalize measured signals to 100% helps improve accuracy for laser ablation applications where matrix matched calibrations are not available.

Figure 1. Agilent 7900 ICP-MS with workstation showing latest version of Agilent ICP-MS MassHunter software.

ICP-MS Analysis of Heavy Metals and Other Trace Elements in Alternative Proteins Per US FDA EAM 4.7

Webinar review by Jenny Nelson and Ed McCurdy, Agilent Technologies, Inc.

Demand for plant-based and other non-animal sources of protein

Growing populations and increasing prosperity are driving demand for meat in many countries. At the same time, many people are becoming more aware of the health benefits of lower meat consumption, and more concerned about the environmental impact of intensive livestock farming. The combined effect is increasing demand for alternative protein sources, including plants and algae, fungi, insects, and cultured (lab-grown) meat.

The food industry is responding by developing new products, many of which use novel ingredients and processes. As with traditional food production, these new foods must be monitored for contaminants, including heavy metals and other trace elements, to ensure consumer safety and nutritional quality.

ICP-MS analysis of alternative protein foods

While regulations specific to alternative proteins are not yet well established, the existing regulatory framework for foods includes methods that are applicable. For example, US FDA Elemental Analysis Manual (EAM) 4.7 (*1*) defines an ICP-MS method for the determination of arsenic, cadmium, chromium, lead, mercury, and other elements in foods after microwave digestion. EAM 4.7 can be used for the multi-element analysis of alternative proteins, as explained in a recent webinar presented by Agilent experts Tarun Anumol, Jenny Nelson, and Peter Riles. Available on demand at: Measuring Heavy Metals and Other Elements in Alternative Proteins

In the webinar, Tarun described the current status and predicted growth of the alternative protein market and discussed key sources of non-animal protein. Jenny and Peter then explained the analytical requirements for nutrients and potentially toxic trace elements in food. They went on to present details of ICP-MS methods that can be used for the analysis of alternative proteins.

Jenny presented Agilent 7850 ICP-MS method validation results for EAM 4.7 and showed data demonstrating routine analysis over 48 hours. Jenny also presented results for cell culture media used to grow cultured meat (*2*). Food manufacturers monitor the nutrient levels and trace element concentrations in cell culture media to ensure optimum utilization of this expensive resource.

Peter presented ICP-MS data for non-meat protein products, including cricket powder, reishi mushroom, blanched almond meal, and besan flour. Certified reference materials for these sample types are not available yet, but performance was confirmed by spike recoveries and accurate results for other food CRMs.

Conclusion

The alternative protein market is growing rapidly, and producers and regulators need validated methods to ensure product quality and safety. Applicable methods for trace elements include EAM method 4.7 for ICP-MS.

References

1. Patrick J. Gray, William R. Mindak, John Cheng, US FDA Elemental Analysis Manual, 4.7, Final version 1.2 (February 2020), accessed September 2022, https://www.fda.gov/media/87509/download
2. Determination of Heavy Metals and Trace Elements in Alternative Meats Per EAM 4.7 Method for ICP-MS, Agilent publication 5994-5181EN

New Functions and Features in Agilent ICP-MS MassHunter Software Revision 5.2

Glenn Woods and Ed McCurdy, Agilent Technologies, Inc.

New revision of ICP-MS MassHunter software

Agilent ICP-MS MassHunter software provides instrument control and data analysis (DA) for Agilent ICP-MS and ICP-QQQ systems. The latest revision of ICP-MS MassHunter, version 5.2, was released in September 2022. ICP-MS MassHunter 5.2 supports all current 7850 and 7900 single quadrupole ICP-MS and 8900 ICP-QQQ systems and is also compatible with the 7700 and 7800 ICP-MS and 8800 ICP-QQQ instruments.

The new revision of ICP-MS MassHunter includes updated drivers for integrated control of Agilent LC and GC systems. Direct control of Agilent 8890 GC systems is now provided, as well as the Agilent 7890 GC.

ICP-MS MassHunter 5.2 also enables monitoring and control of the Agilent Durachill water chiller (G8414A). The software provides a real-time readout of chiller status (offline, standby, running), control of the set temperature, and error status such as low chiller fluid. Automatic switching on and off of the chiller, triggered by the ICP-MS state, is also supported.

New features in revision 5.2

ICP-MS MassHunter version 5.2 builds on the new, simplified user interface introduced in version 5.1, with a host of enhancements and new functions, including:

Support for multi-injection Compound Independent Calibration (CIC) for chromatography

In ICP-MS chromatographic methods, unknown compounds can be calibrated using an approach known as compound independent calibration (CIC), where the calibration is generated from the elemental response measured for several different compounds.

In ICP-MS MassHunter 5.2, the CIC calibration can be created from multiple compounds, even if they are measured in different samples. Options for finding and integrating unknown peaks have also been enhanced.

Further improvements for nanoparticle (NP) analysis

Previous versions of ICP-MS MassHunter were limited to measuring 16 elements in NPs in a sample. With version 5.2, analysts can now set up the single NP (sNP) method to acquire a virtually unlimited number of elements. Measurement of the elements occurs sequentially during one visit to the sample vial.

Other enhancements in version 5.2 include:

- A new user interface to define the analyte list and calibration information. The display allows switching between simple and detailed views.
- Functionality to correct measured data to sum to 100%, which is very useful for laser ablation.
- Improvements in the workflow for data security for FDA-compliant installations.
- Improved support for building LAN connection.

More information at: Agilent ICP-MS software | Agilent

ICP-MS MassHunter 5.2 compatibility

As well as the ICP-MS mainframes already listed, ICP-MS MassHunter version 5.2 is compatible with:

- Windows 10 Pro or Enterprise (64 bit) v.21H2.
- Microsoft Excel. Although ICP-MS MassHunter does not require Excel, it is fully compatible with 32-bit Excel 2021. Excel 2019 is also supported.
- Agilent and third-party* autosamplers and accessories (*using plug-ins from the accessory supplier).
- Agilent 7890 & 8890 GC and 7693 autosampler. Requires the optional chromatographic software module.
- Most Agilent 1100 and 1200 Series HPLC modules and peripherals. Requires the optional chromatographic software module.
- Agilent compliance software, OpenLab Server and ECM XT 2.6/2.7, ECM 3.5/3.6, SDA B.02.02.

Ultratrace Analysis of Dissolved and Particulate Contamination in Semiconductor Grade NMP

Yoshinori Shimamura, Agilent Technologies, Inc., Tokyo, Japan. Sample analysis performed in collaboration with Kakeru Usuba, Naoki Katano, and Takao Shibasaki of FUJIFILM Wako Pure Chemical Corporation, Japan

Trace level analysis of semiconductor chemicals

Semiconductor manufacturers strive to develop novel materials and processes to increase the performance of microelectronics while simultaneously reducing device size, power consumption, and heat generation. These advances require continual improvement in the purity of manufacturing process chemicals. Since its launch in 2012, triple quadrupole ICP-MS (ICP-QQQ) has been accepted as the standard technique for monitoring elemental contamination in semiconductor chemicals.

Dissolved element levels are routinely monitored during integrated circuit (IC) manufacturing. But semiconductor manufacturers and chemical suppliers must also control particulate contamination, especially metallic particles—including nanoparticles (NPs)—which can cause circuit defects and device failure. NPs can be introduced from raw materials and from processing equipment.

SEMI develops and publishes specifications and test methods to support semiconductor industry requirements, including defining methods to assess the levels of particulate contamination in ultrapure water (*1*). Some semiconductor manufacturers are already routinely monitoring levels of particulate contamination using techniques such as laser particle counters. But particle counters cannot identify which elements the NPs contain, which is becoming a priority for the industry.

ICP-MS can measure the number, size, and composition of NPs, using a technique called single particle (sp-)ICP-MS. The key requirements for NP analysis are very high sensitivity and fast acquisition speed. High sensitivity (or, more accurately, high signal-to-noise, S/N) is essential to allow the counts from individual NPs to be distinguished above the background. Fast data acquisition enables multiple measurements to be collected during the short-lived signal pulse that is generated as each individual NP is decomposed as it passes through the plasma.

Dissolved and particulate contaminant analysis

Agilent ICP-MS systems provide fast, sensitive NP analysis as well as dissolved element quantification, giving a total analysis solution for semiconductor labs. From Agilent ICP-MS MassHunter software revision 5.2, analysts can now set up spICP-MS methods to monitor a virtually unlimited number of analytes in NPs in each sample, as shown in Figure 1. Different NP elements are measured sequentially, each under optimum conditions.

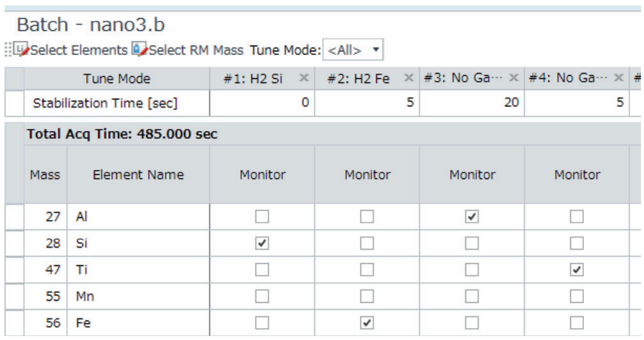


Figure 1. Agilent ICP-MS MassHunter 5.2 setup of sp acquisition.

Advances in semiconductor manufacturing mean that industry practice often outpaces the development of new standards. For example, the current specification for the highest purity of n-methyl-2-pyrrolidone (NMP), SEMI C33-0213 Grade 3, which dates from 2013, specifies contaminant levels of 5 ppb or higher (*2*). But chemical suppliers and IC manufacturers are already working to contaminant levels of <20 ppt in NMP, which is orders of magnitude lower than the Grade 3 standard.

An Agilent 8900 ICP-QQQ was used to measure dissolved contaminants and NPs in EL (for Electronics industry) and SP (supreme pure) Grade NMP samples provided by FUJIFILM Wako Pure Chemical Corporation, Japan (*3*). Concentrations of 54 dissolved elements, including all 22 elements listed in SEMI C33-0213, were quantified using the method of standard additions (MSA) (*4*).

Multielement NP characterization of NMP

Following an initial screening acquisition to identify potential particulate contaminants, a multielement NP method was set up to measure particles containing 14 elements in the two grades of NMP using spICP-MS. An Agilent 8900 Triple Quadrupole ICP-MS (ICP-QQQ) was used for the analysis. Figure 2 shows the size distribution of the elements detected in particles measured in the two samples. The much lower particle number and absence of larger particles in the SP grade sample confirm the much higher purity of this higher-quality reagent.

Conclusion

Agilent ICP-QQQ is a standard technique used for monitoring dissolved elemental contamination in semiconductor manufacturing process chemicals. New software developments have extended the multielement NP analysis capability of the Agilent 8900 ICP-QQQ for routine monitoring of particle contamination.

The 8900 ICP-QQQ offers a unique combination of extremely high sensitivity, ultralow background, fast time resolved data acquisition, and exceptional control of spectral interferences. These capabilities make the 8900 the ideal tool to monitor ultralow level contaminants and NPs in the highest purity process chemicals used in advanced semiconductor manufacturing.

References

1. SEMI F104 - Test Method for Evaluation of Particle Contribution of Components Used in Ultrapure Water and Liquid Chemical Distribution Systems
2. SEMI C33-0213 - Specifications for n-Methyl 2-Pyrrolidone, accessed September 2022, https://store-us.semi.org/products/c03300-semi-c33-specifications-for-n-methyl-2-pyrrolidone
3. High-purity Solvent and Acid, FujiFilm Wako Pure Chemical Corporation, accessed October 2022, https://labchem-wako.fujifilm.com/us/category/00282.html
4. Elemental and Particle Analysis of N-Methyl-2-Pyrrolidone (NMP) by ICP-QQQ, 5994-5365EN

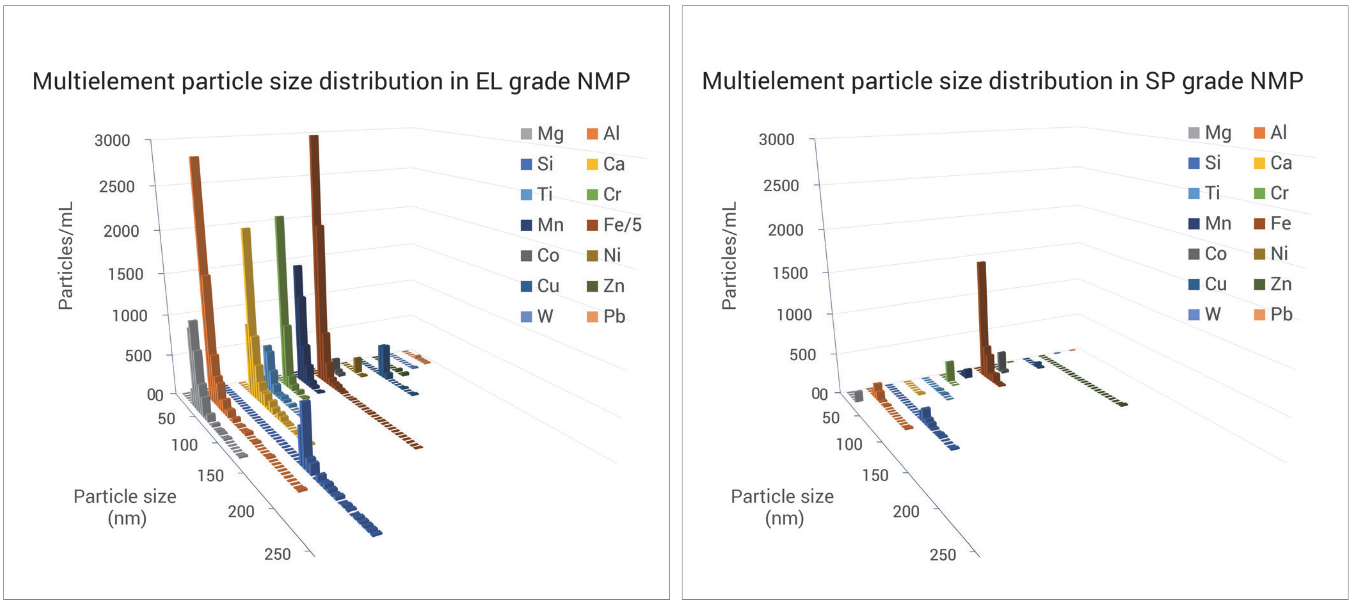


Figure 2. Metallic particle size distribution for 14 elements in two grades of NMP: EL (for Electronics industry) and SP (supreme pure) grade. Note the number of Fe particles measured in EL grade NMP has been divided by five to fit on the same scale as the other elements.

New Multi-Injection Compound Independent Calibration and Sum to 100% Functions in ICP-MS MassHunter

David Gemeinder, Matthias Steiner, Simon Treu, Christian Wolf, Peter Leonhard, Merck KGaA, Darmstadt, Germany. Naoki Sugiyama, Ed McCurdy, Glenn Woods, Agilent Technologies, Inc.

Advanced application features in version 5.2

Each new version of Agilent ICP-MS MassHunter software introduces new features and functionality, while often also simplifying workflows and improving the integration of accessories and peripherals. ICP-MS MassHunter version 5.2 contains a range of improvements, including:

- Extension of the single nanoparticle functionality to allow a practically unlimited number of masses to be measured in each sample (see separate article).
- Enhancement of the Compound Independent Calibration function to use data from multiple compounds measured in multiple sample injections.
- A new "Normalize to 100%" function to allow correction of measured concentrations to give totals relative to the sum of all measured elements.

Multi-injection Compound Independent Calibration

ICP-MS is used as the detector for many elemental speciation applications, typically in combination with HPLC (LC-ICP-MS) or gas chromatography (GC-ICP-MS). ICP-MS offers many benefits, including extremely high sensitivity, low and uniform background, near-universal elemental coverage, and wide dynamic range.

A further, unique benefit of ICP-MS as a chromatographic detector is that the ICP plasma ion source operates at a very high temperature. This high temperature means the plasma provides consistent ionization of the elements in each target compound, regardless of the structure and chemical properties of the individual compound. This means that ICP-MS does not suffer from the limitation — typical for other chromatographic detectors — that each target compound must be calibrated based on compound-specific standards for that compound. Non-specific or compound independent calibration (CIC) is based on the ICP-MS signal for heteroelements in each compound. For example, the organophosphate pesticide phorate ($C_7H_{17}O_2PS_3$) contains both P and S. Any compound that contains a known amount of an element can be used as a standard to calibrate other, unknown, or uncalibrated compounds that contain the same element.

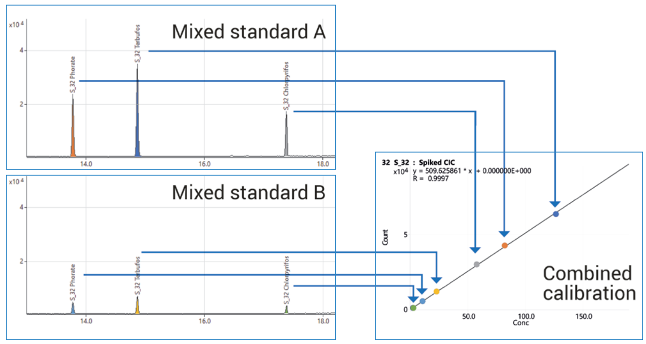
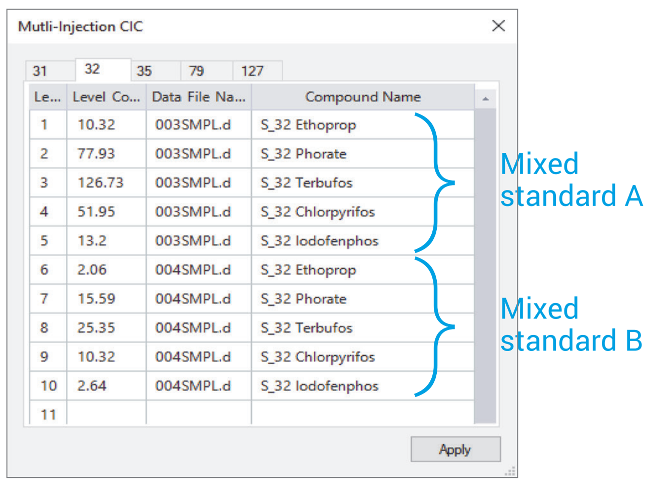


Figure 1. A multi-injection CIC is derived from the elemental signals for different compounds measured in multiple injections.

The principle of CIC is illustrated in Figure 1, and the ICP-MS MassHunter setup screen for sulfur-based compounds (measured at mass 32) is shown in Figure 2.



Le...	Level Co...	Data File Na...	Compound Name
1	10.32	003SMPL.d	S_32 Ethoprop
2	77.93	003SMPL.d	S_32 Phorate
3	126.73	003SMPL.d	S_32 Terbufos
4	51.95	003SMPL.d	S_32 Chlorpyrifos
5	13.2	003SMPL.d	S_32 Iodofenphos
6	2.06	004SMPL.d	S_32 Ethoprop
7	15.59	004SMPL.d	S_32 Phorate
8	25.35	004SMPL.d	S_32 Terbufos
9	10.32	004SMPL.d	S_32 Chlorpyrifos
10	2.64	004SMPL.d	S_32 Iodofenphos
11			

Figure 2. Multi-injection CIC setup table for mass 32 (S) in ICP-MS MassHunter.

The data from multiple compounds from separate standards can be combined to give a CIC "elemental response" calibration, based on the ^{32}S signal in this case.

The CIC can be used to calibrate any sulfur-containing compound, as shown in the plot in Figure 3.

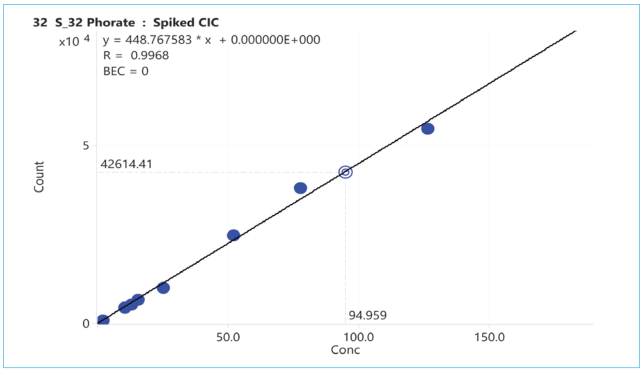


Figure 3. Ten-point multi-injection CIC for quantification of phorate based on sulfur response in two standards each with five sulfur-containing compounds.

Normalize to 100% function for laser ablation

In laser ablation (LA-)ICP-MS applications, the analysis often includes all the elements, including the matrix element(s). This gives users the option to normalize all the measured concentrations to 100%, which gives more accurate correction for variable ablation yield than can be achieved using simple internal standardization.

The correction uses an add-in, activated in the Data Analysis (DA) Tools menu, to control the correction and setup the calibration, as shown in Figure 4.

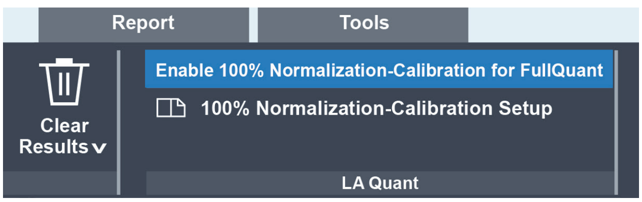


Figure 4. 100% normalization function enabled in ICP-MS MassHunter version 5.2.

ICP-MS measures elemental signals, while the elements in samples are often not present in their elemental form. For example, silicon in glass is present as SiO_2. Si has an atomic weight of 32.07, while O has an atomic weight of 16, so only half the mass of SiO_2 (32/64) is elemental Si. To provide accurate correction to 100%, the DA calculation must be able to convert from the element signal to the compound concentration and *vice versa*. Setup simply requires the user to enter the actual compounds into the calibration table, so the conversion can be applied during the normalization.

The new 100% normalization function was used for the analysis of trace elements in certified reference material ERM-EB385 Pure Copper, standardized against NIST 612 Glass. The concentrations determined in the Cu CRM, after 100% normalization are shown in Table 1, together with the recoveries compared to the certified values.

Table 1. Copper CRM results (ppm) and recoveries with 100% normalization.

Element	Certified	After 100% Normalization	Recovery (%)
Cu		999,543 (99.95%)	
Ag	28.6	28.24	98.7
Al	28.6	28.06	98.1
As	11.4	11.85	103.9
Bi	5.81	4.6	79.2
Cd	5.8	6.71	115.7
Co	6.93	5.89	85.0
Cr	9.81	8.14	83.0
Fe	45.4	40.53	89.3
Mg	29.1	24.59	84.5
Mn	10.1	8.24	81.6
Ni	11.9	11.17	93.9
P	12.9	13.48	104.5
Pb	11.3	10.28	91.0
S	31.3	27.25	87.1
Sb	19.1	20.75	108.6
Se	7.2	4.47	62.1
Sn	18	15.97	88.7
Te	10	11.74	117.4
Ti	3.83	3.41	89.0
Zn	58	66.4	114.5

The results in Table 1 demonstrate accurate quantitative analysis for the certified elements in Pure Copper CRM EB385. Almost all recoveries were between 80 to 120%, without using a matrix matched standard. The new 100% normalization function greatly simplifies calibration strategies for LA-ICP-MS applications.

Conclusion

The latest revision of ICP-MS MassHunter software includes many new features to improve functionality and usability in conventional applications. In addition, the new single NP capability, multi-injection CIC, and 100% normalization functions improve performance and add flexibility for NP, chromatography, and LA applications.

European Winter Conference on Plasma Spectrochemistry, Ljubljana, Slovenia, Jan 29 to Feb 3, 2023

Join Agilent Technologies Atomic Spectroscopy team in Ljubljana at the 2023 Winter Conference on Plasma Spectrochemistry, https://ewcps2023.si/

Agilent will be presenting technical posters on ICP-MS and ICP-OES for a range of applications including:

- Renewable energy and Li-ion battery technology
- Novel, non-animal source alternative protein sources and their safety
- Measuring ultra-low levels of dissolved and particulate contaminants in high purity chemicals and materials

There will also be an opportunity to meet Agilent technical and applications specialists and expert users for informal discussions at social events including a lunch seminar. Look out for further details in future communications.

We are looking forward to seeing many Agilent ICP-MS and ICP-OES users in January 2023!

Latest Agilent ICP-MS publications

- **Featured article in Spectroscopy:** Agilent 7900 for seawater analysis, Spectroscopy Supplement, September 1, 2022, 37, S9, 16–22, ICP-MS Configuration and Optimization for Successful Routine Analysis of Undiluted Seawater
- **Application note:** Determination of Heavy Metals and Trace Elements in Alternative Meats Per EAM 4.7 Method for ICP-MS, 5994-5181EN
- **Application note:** Elemental Analysis of Chemically Defined Cell Culture Media by ICP-MS, 5994-5355EN
- **Application note:** Characterization of Synthesized Iron Nanoparticles in Hydrocarbon Matrices by Single Particle (sp)ICP-MS, 5994-5322EN
- **Application note:** Analysis of Bromine Pesticide Residue in Australian Grain Export Cargoes Using ICP-MS, 5994-5349EN
- **Application note:** Analysis of Metallic Impurities in Specialty Semiconductor Gases Using Gas Exchange Device (GED)-ICP-MS, 5994-5321EN
- **Application note:** Accurate ICP-MS Analysis of Elemental Impurities in Electrolyte Used for Lithium-Ion Batteries, 5994-5363EN
- **Application brief:** Quantifying Metal Impurities in Li-Ion Battery Raw Materials by ICP-MS/MS, 5994-5341EN

Published in the USA, October 20, 2022
5994-5303EN
DE96475495

Agilent
Trusted Answers