ICP Standards – Relevance, Application and Metrology

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Abstract

The measurement of cations and anions is of critical importance in almost every industry. Detailed examples of these industries, whilst not exhaustive, are presented in this paper and this list is stealthily growing. The level of user expectation in terms of sensitivity of the main methods for measurements stealthily growing, as is the necessity for versatility and efficiency. Therefore, methodologies such as spectrophotometry, flame photometry, ion selective electrodes and atomic absorption, although all still relevant and important are giving way to ICP-OES and ICP-MS techniques. Basic information on the measurement principle and functionality coupled with detailed information on the features, benefits, advantages and disadvantages of these two instrumental techniques are presented and the descriptions are augmented by some easy to follow graphics and diagrams. Ultimately though, almost all instrumental analytical techniques are comparative and therefore require high quality calibration, verification, tuning and quality control standards. There are several excellent producers of such standards that have offerings in the marketplace but in order to enable the analyst to understand and choose what criteria a high-quality standard must fulfil, the standards available from Reagecon are used as a case study. This case study details the difference between external, internal and tuning standards, and also details the meticulous manufacturing and testing processes necessary to practice these high value-added products. This paper places particular emphasis on the metrology relating to ICP Standards, particularly purity, traceability, measurement uncertainty and certification using the products produced by Reagecon as real life examples. For additional information on extra features, benefits and options, a brief list of references is included. Much more product information can be obtained at www.reagecon.com

Introduction

The measurement of cations and anions is of critical importance in almost every industry. The extent of these industries is almost limitless but can broadly be classified as Industrial Engineering, Agriculture, Food, Pharmaceutical, Mining and Geology, Medicine and Medical Devices, Petrochemicals, Metal Processing and Environmental Measurement. In fact, it would be difficult to name an area of science, medicine or engineering that does not require such measurement. Later, in this document, we will take a more detailed look at some of these industry sectors. (Table 1)

Technological advances, regulatory requirements and customer expectations now dictate that over the last 40 years, the level of sensitivity of such measurements has increased from an expectation of parts per thousand to parts per trillion which is a nine-fold order of magnitude. This has dictated that instrument manufacturers and standards manufacturers face increasingly complex technological challenges. Forty years ago, methods of choice for measuring cations and anions included colourimetric measurement, flame photometry, ion selective electrodes and atomic absorption spectroscopy. All of these technologies are still widely used but nowadays where greater sensitivity, versatility or efficiency are required, ICP-OES, ICP-MS, ion chromatography and XRF are widely used. The focus of this publication will be ICP-OES and ICP-MS, which will include a brief description of the underlying technology, features and benefits.

The use of such instruments requires standards that are more accurate, pure, stable, available in a variety of matrices and able to co-exist in multi element formulations. Several companies have risen to the technological challenges that the manufacture of such standards demand and produce a wide variety of standards for these technologies. Significant technical detail will be presented later on such standards. The standards produced by Reagecon will be used for example purposes in order to demonstrate what aspects of such products the user needs to take cognisance of, when undergoing a procurement process for standards.

To start with, I will describe what ICP-MS is, the components of a typical ICP system, the advantages and disadvantages of ICP-MS and how it compares technically with other elemental techniques. I will then, present details of Reagecon's ICP Standards that include how the products are produced and tested, and what features and benefits this production and testing regime confers on you, the user of the product. (Barron, 2016)

ICP-MS, Technology and Functionality

The Principle of Measurement

Inductively Coupled Plasma – Mass Spectrometry (ICP-MS) is an analytical technique used for elemental determinations. Put simply ICP is used to atomise and ionise the sample using an Argon plasma and RF coil. The MS is then used to separate and detect ions by their mass-to-charge (M/Z) ratio.

The ICP-MS Instrument

Following the introduction of the sample, ions are generated in the ICP, there is a plasma vacuum interface, which is followed by ion focussing. This is in turn followed by separation of the ions and then measurement (see Diagram 1).

Schematic of a typical ICP-MS Instrument

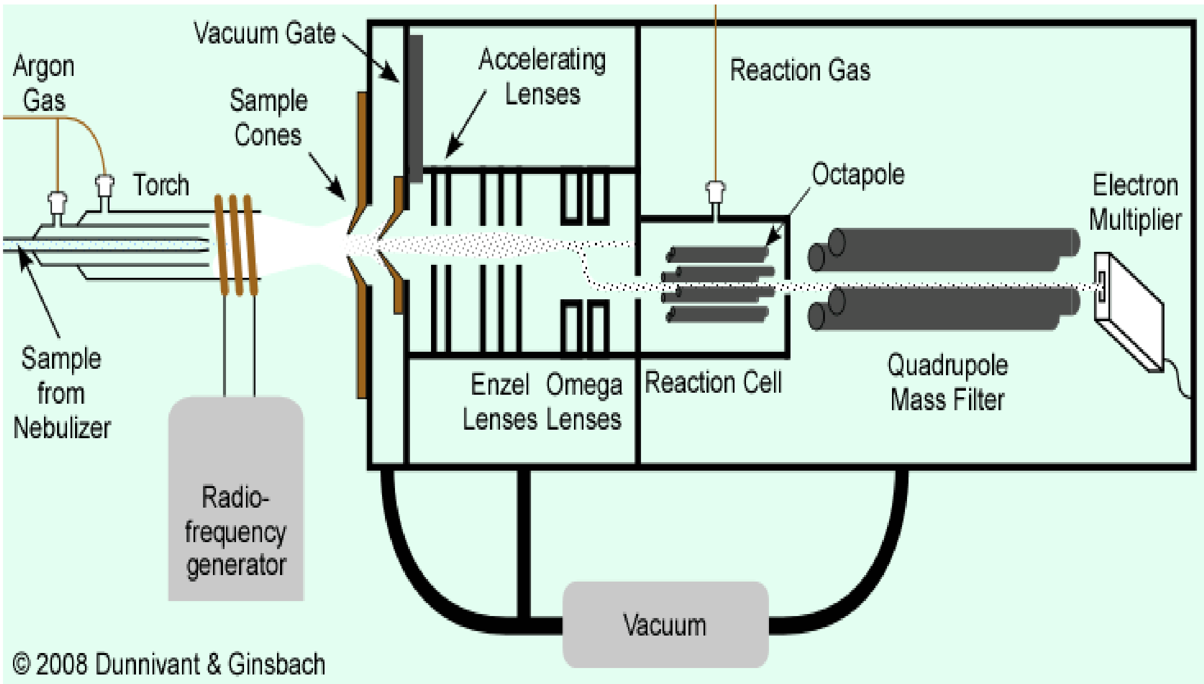

Diagram 1

Mass Spectrometry

Then the material enters the mass spectrometer, it is subjected to light and heat energy from a high energy source called the plasma, which ejects the electrons from their outer shells. The result is a free electron and an atom with a positive charge, which is measured directly in the mass spectrometer as an ion (see Diagram 2).

Schematic of a typical Mass Spectrometer

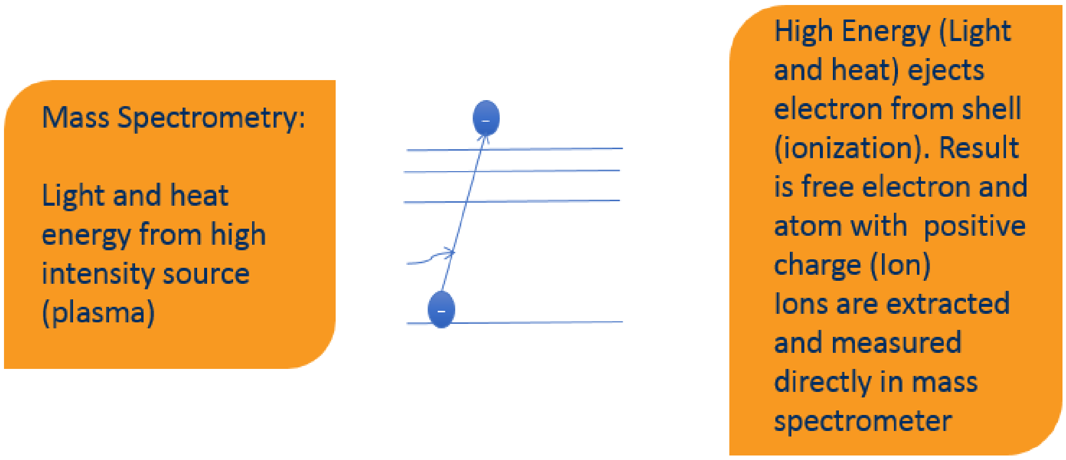

Diagram 2

ICP-MS Advantages and Disadvantages

ICP-MS is a highly sensitive and versatile tool that offers the user many advantages:

- A requirement of a small sample size
- An excellent dynamic range
- Accommodation of organic solvents
- A multi-elemental technique
- Can perform isotope differentiation and determination
- Can perform scanning (semi-quant) functionality
- Offers a superior limit of detection to any other analytical methods for cations
- All the interferences are limited and well defined
- The most significant disadvantage is that it is a costly capital spend.

ICP-MS photographed in the Reagecon Cation Test Laboratory

Photograph 1

ICP-OES – Technology and Functionality

The Principle

This is a simpler technique and is often referred to as ICP. It is a multi-element analysis technique that uses an inductively coupled plasma source to dissociate the sample into its constituent atoms or ions, exciting them to a level whereby they emit light of a characteristic wavelength. A detector measures the intensity of the emitted light, and calculates the concentration of that particular element in the sample. (See Diagram 3). When undergoing ICP analysis, the sample experiences temperatures as high as 10,000 degrees celsius, where even the most refractory elements are atomized with high efficiency. As a result, detection limits for these elements can be orders of magnitude lower with ICP than with Flame Atomic Absorption Spectroscopy techniques, typically at the 1-10 parts-per-billion level.

There are two different types: radial and axial.

In the traditional radial configuration, the plasma source is viewed from the side, across the narrow emitting central channel of the plasma. Many newer systems view the emitting channel horizontally along its length; this is known as the axial method. Axial viewing increases the path length and reduces the plasma background signal, resulting in detection limits as much as 5-10x lower than with the radial configuration.

Schematic of a typical ICP-OES Instrument

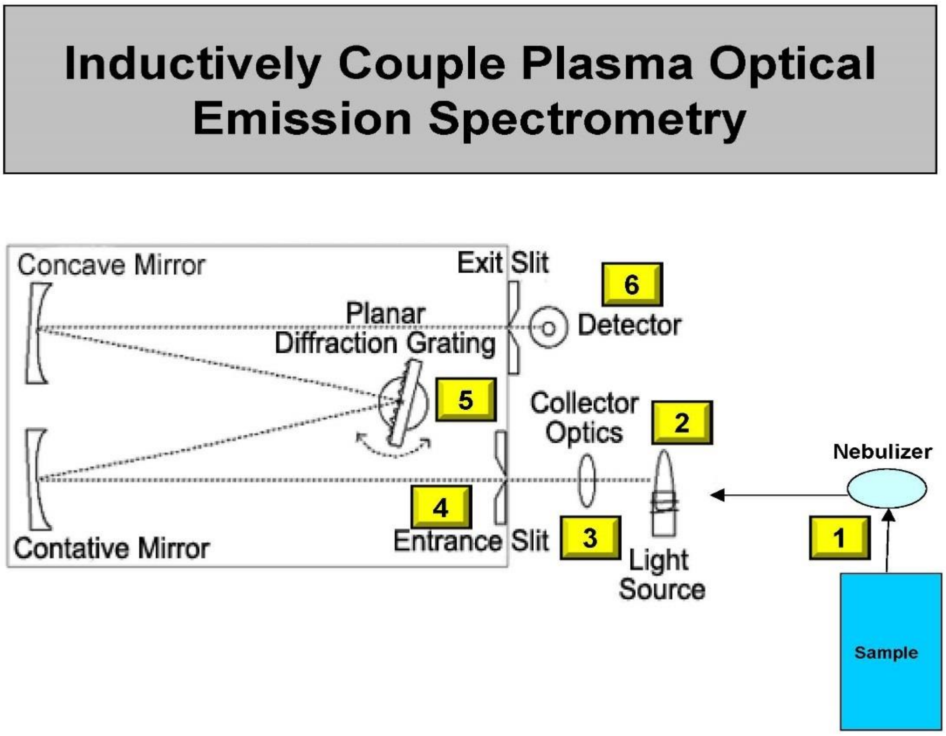

Diagram 3

ICP-OES Advantages and Disadvantages

Although ICP-OES does not have as many advantages as ICP-MS and more disadvantages, it is a widely used technique and provides a fit for purpose solution in most instances. Of course, you may use an instrument that measures several elements simultaneously, a simultaneous ICP-OES system or one that measures sequentially – a sequential ICP-OES. It is a good general-purpose technique, has good dynamic range, accommodates organic solvents and it a multi-elemental technique. However, the cost of the instrument is high and limits of detection are not as good as ICP-MS. There are also higher sample volume requirements and spectral interferences for unknown/complicated matrices.

Comparison of Elemental Techniques

It is worth having a brief look at how sequential and simultaneous ICP-OES compares, how either compares with ICP-MS and how ICP in general compares with Graphite Furnace AAS. (See Diagram 4 and Diagram 5)

Features and Benefits Comparison of GFAAS and ICP Instruments

		Sequential	Simultaneous	
Criteria	**GFAAS**	**ICP-OES**	**ICP-OES**	**ICP-MS**
Detection Limits	ppt	ppb	ppb	ppb-ppt
Linear Range	2-3	4-6	4-6	9*
Interferences	Moderate	Many	Many	Few
Speed	Slow	Slow	Fast	Fast
Elemental coverage	Poor	Good	Good	Excellent
Multi-element	No	Yes	Yes	Yes
Simultaneous	No	No	Yes	Yes
Sample size	µL	mL	mL	µL or mL
Capital cost	Low	Low	Moderate	High
Operating cost	High	Moderate	Moderate	Low

Diagram 4

A short graphic comparison between the limit of detection and throughput of Flame AA, Graphite Furnace AA, ICP-OES and ICP-MS.

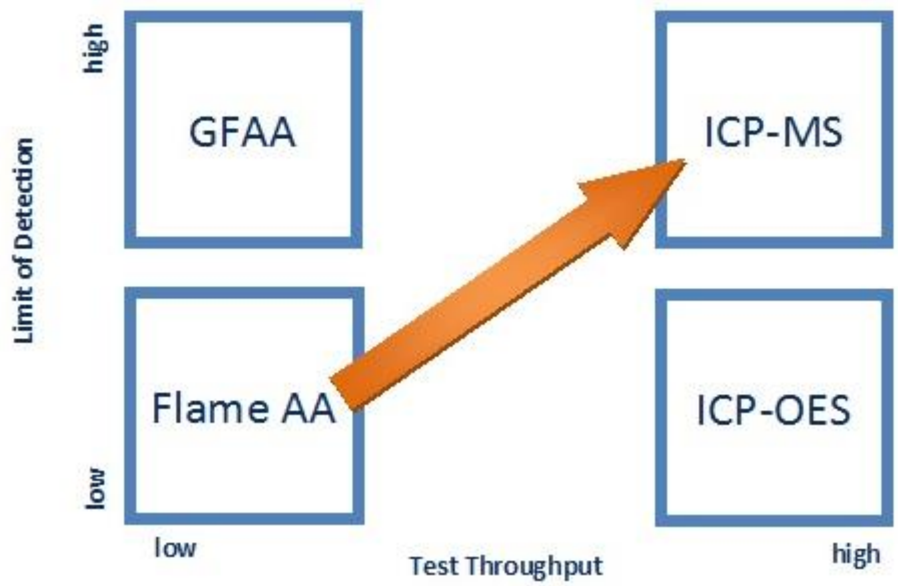

Diagram 5

Standards for Calibration and Tuning of ICP-MS and ICP-OES Instruments

Ultimately, the quality of any analytical result, its fitness for purpose, its correctness and the proof of that correctness is entirely dependent on the standards used. ICP measurement, in any of its forms is no exception to that rule. Let us now look at a number of different types of ICP-OES/ICP-MS standards as follows:

- External Calibration Standards
- Tuning Standards
- Internal Calibration Standards

Later we will look at how these standards are produced, tested, verified and certified, with particular focus on the exacting nature of all of these steps in the context of ICP and ICP-MS. Finally, we will talk all about the myriad of concentrations, packaging options, element mixes and customisation options available from Reagecon.

External Calibration Standards

Almost all analytical test methods are comparative, which means the analyst compares a known or series of knowns, which are the calibration standards with an unknown, which is the sample. In the case of ICP, a calibration curve is established and the concentration of the unknown is established from this curve. It is an imperative that the standards and samples are prepared in exactly the same way.

A typical calibration curve is presented here where intensity on the Y axis is plotted against concentration on the X axis and thus the concentration of the unknown sample is a function of the intensity of that sample.

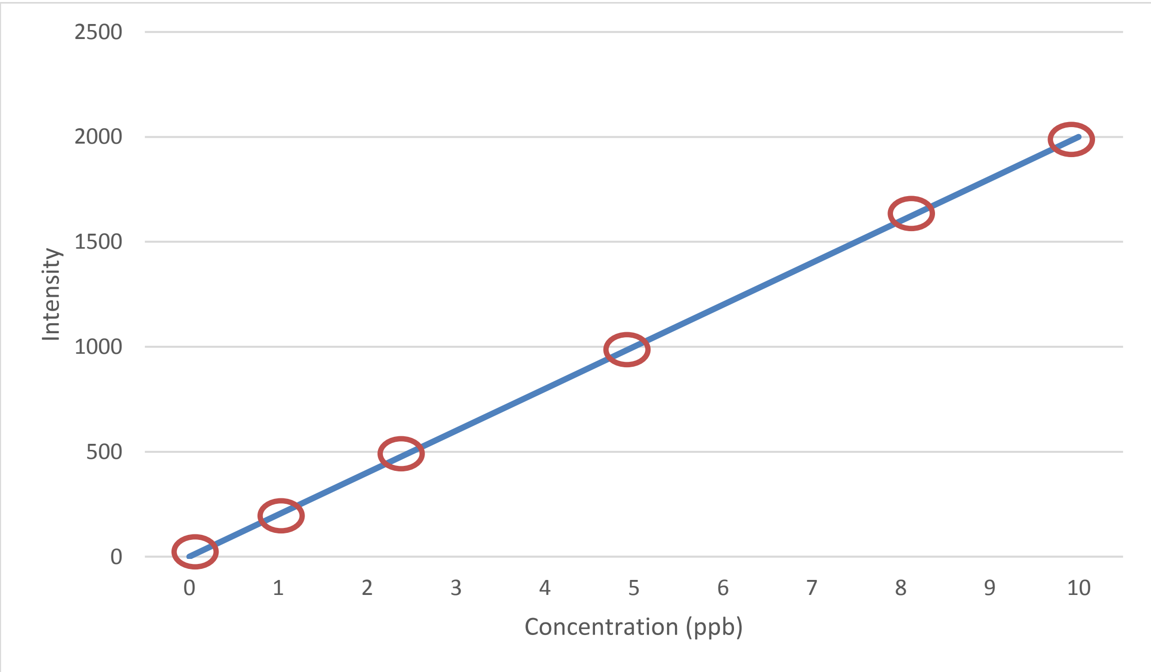

Diagram 6

Internal Calibration Standards

ICP-MS is a highly sophisticated instrument and requires the use internal standards. Careful study of the matrix effect in ICP-MS showed that, in all cases studied, the magnitude of the signal suppression or enhancement depends in a regular way on the mass number. Hence, accurate correction for non-spectral interferences is only possible using an internal standard with a mass number close to that of the analyte element or elements. To obtain optimal precision and accuracy, the selected internal standard should be as close in mass number as possible to that of the analyte element(s). When a number of elements over a considerable mass range are to be determined, several internal standards or a multi-element internal standard has to be used.

It is also shown that using an internal standard with mass number close to that of the analyte improves precision. ICP-MS Internal Standards typically contain a number of elements spread out across the mass range e.g. Lithium (Mass 6), Scandium (45), Germanium (72), Yttrium (89), Rhodium (103), Indium (115), Terbium (159) and Bismuth (208).

Tuning Standards

Likewise, a sophisticated instrument such as an ICP-MS needs the use of Tuning Standards. Every time it is used you need to verify it is tuned properly. So, a Tuning Solution must be run every time the plasma is lit before any analysis can take place. The Tuning Solution's role is to "Tune" the Hardware of the instrument to ensure that it is running correctly. Tuning Solutions verify that the resolution and mass calibration of the instrument are within the required specification. ICP-MS Tuning solutions contain elements that cover the mass range of the instrument. For example, a typical Tuning Solution might contain the following elements and mass numbers:

Lithium (Mass 7), Cobalt (59), Yttrium (89), Cerium (140) and Thallium (205).

The Manufacture of ICP-MS and ICP-OES Standards

The Starting Materials

Reagecon's standards are manufactured in a highly controlled Class 10,000 (ISO 7) cleanroom environment using High Purity starting materials. At least 33 are pure metals of 99.999% purity, others are 99.995% pure and salts where used are 99.99% pure. We also use Ultra-Pure water, High Purity matrix materials, Pre-leached and pre-cleaned bottles. The ultra-pure water is produced by a special proprietary process.

The Raw Materials Testing

All raw materials are assayed by Titration and ICP-MS. This allows the 2 methods to be cross checked against each other, provides 2 layers of traceability because separate CRM's are used to calibrate or control. This quantifies the level of combined impurities in the starting material. The product is then manufactured gravimetrically using the mass balance approach. 100% - sum of impurities (w/w). All measurement uncertainties are collated according to Eurachem/Citac. The results are reported as expanded uncertainties at 95% confidence level. Several of the Reagecon test methods are accredited.

Final Assay and Result

Each batch of finalised ICP standard is assayed on ICP-MS prior to bottling. This verifies the target elements and that the level of impurities has not changed. The results are reported and certified in mg/Kg and mg/L on the basis of weight and density. All volumetric, titrimetric and gravimetric functions are carried out under a highly regulated temperature regime. Reagecon holds ISO17025 accreditation for temperature calibration (density measurements are highly temperature dependent) and the density measurement performed using an oscillating U-tube method in accordance with ASTM D4052-09 method and density method using Bingham Pycnometry.

The Matrix

Although in a lot of cases, there are no technical reasons why one matrix is chosen over another, there are instances where the choice is important. It is important to remember that where there are technical reasons why a particular matrix choice for a standard is important, that reason may also be applicable to the sample. So, the following brief information is offered by way of guidance.

Nitric Acid (HNO_3) is the most commonly used matrix, due to the solubility of the nitrides and the oxidising ability of the nitric acid. There is relative freedom from chemical and spectral interferences as compared to acids that contain Chlorine, Sulfur, Fluorine or Phosphorus.

Hydrochloric Acid (HCl) is the next most common matrix. HCl is volatile and may be corrosive to the instrument, in particular its electronic and metal parts. Exposure of HCl to these parts should be kept to a minimum.

Hydrofluoric Acid (HF) requires HF resistant introduction systems such as Teflon. These systems are more expensive, have lower washout times and deliver a less precise result. However, this acid is an imperative for the dissolution of certain elements, particularly in a multi-element mixture.

Sulphuric Acid (H_2SO_4) is commonly used in sample preparation. Dilutions of Mercury and Gold below 100ppm in Sulphuric Acid should be stored in glass only.

Phosphoric Acid (H_3PO_4) although not commonly used, won't adversely affect most elements but attacks glass and ceramics.

Water (H_2O) Standard solutions in water may be contaminated by micro-organisms, so stability levels are inferior to an acid matrix.

Target Markets for ICP-MS and ICP-OES Standards

In the introduction, we alluded to the wide range of industries to which the measurement of metals using ICP-MS is relevant. In the following table (Table 1), we have presented in more granular detail, not only the broad industry sectors to which the measurement of metals is relevant, but also details of various segments within these industries. We fully realise, that no list is ever totally exhaustive, so we have restricted ourselves to presenting, what we believe from our experience, the main target markets are.

Main Target Markets for where ICP-OES and ICP-MS is relevant

Target Markets	
Industrial Engineering	Any company casting or manufacturing metal parts from raw materials e.g. airplane bodies
	Engine components
	Moving parts
Agriculture	Soil
	Dairy products
	Plant and animal tissue
	Veterinary diagnostics
	Animal feeds
	Animal medicines
	Farming effluent
Food	Solid foods
	Beverages
	Mineral waters
	Food components
	Raw materials
Aquaculture	Water
	Feed
	Effluent
	Medicines
	Tissue
Pharmaceuticals (Barron, 2019. Standards for Elemental Impurities in Pharmaceuticals)	Pharmacopoeia methods
	Raw materials
	API's
	In process materials
	Waste
	Finished liquid and solid base medicines
Mining and Geology	ORE's
	Processed raw materials
	Precious metals
	Geological samples
	Fuels and petrochemical reservoirs
Medicine and Medical Devices	Implants
	Diagnostics
	Dental products
Petrochemicals	Wear & tear oils
	Crude oils
	Petroleum (lead)
	Petrochemical derivatives
Electroplating	
Environmental	Potable water
	Waste water
	Amenity waters
	Surface
	Reservoirs
	Industrial waste streams
Semi-conductors	
Power Stations	Hydro
	Fossil Fuel
	Nuclear
Forensics	Ballistics
	Toxicology
	Crime scenes
Pulp and Paper	

Table 1 (Barron, 2019. Webinar)

Conclusion

Reagecon's offering of ICP Standards is very extensive with many features and benefits which include the following:

- Widest range of options in terms of pack sizes, matrices, single element and multi element mixes
- Extensive metrological features, that includes purity, traceability, measurement uncertainty, stability, certification and accreditations.
- A massive customised offering, available from no other source.
- Extensive free advice on technical features, elemental compatibility, shelf life, sample preparation, shipping, safety and dispatch.
- Full compliance with all regulations, that include REACH, GHS, IATA to name a few.

However, to reiterate, there are many other high-quality producers of such standards.

We have not detailed an emerging market area, which is the measurement of metallic nanoparticles, for which we have developed in this laboratory, a suite of appropriate standards which are subject to patent protection. (Barron et al, 2017)

References

Barron, J., Hynes, M., 2016. Physical and Chemical Standards Compendium, pp. 183-248. ©Reagecon Diagnostics Ltd, Shannon Free Zone, Shannon, County Clare, Ireland

Dunnivant, F., Ginsbach, J., 2009. *Flame Atomic Absorbance and Emission Spectroscopy and Inductively Coupled Spectrometry - Mass Spectrometry.,* Chapter 4.2 Components of a Mass Spectrometer.,

Barron, J., Sychra, V., O'Keeffe, J., 2017. US Patent, Patent No. 9,612,202 B2 2017.

Barron, J., 2019. *ICP Standards Webinar*, ©Reagecon Diagnostics Ltd, Shannon Free Zone, Shannon, County Clare, Ireland

Barron, J., 2019. Standards for Elemental Impurities in Pharmaceuticals.