

Automated, Intelligent Sample Preparation: Integration of the ESI prepFAST Auto-Dilution System with the Thermo Scientific iCAP Q ICP-MS

Julian D. Wills,¹ Christoph Wehe,¹ Shona McSheehy Ducos,¹ Austin Schultz,² and Paul Field²

¹Thermo Fisher Scientific, Bremen, Germany

²ESI, Omaha, USA

Key Words

Auto-Dilution, EPA 200.8, ICP-MS, USP <233>

Goal

To demonstrate the increase in and reduce manual tasks through automation of the analytical workflow. Through an integrated combination of intelligent software and hardware, demonstrate how auto-calibration and auto-dilution can simplify routine elemental analysis.

Introduction

Similar to most solution based techniques, elemental quantification by inductively coupled plasma mass spectrometry (ICP-MS) involves numerous dilution steps before the analytical run can commence.

A series of calibration standards have to be supplied at concentration levels designed to span the expected content in the unknowns. These standards are usually prepared by serial dilution from one or more stock standard solutions. Depending on the required calibration range, several dilutions between 10 to 200-fold are usually required. The majority of samples for elemental analysis by ICP-MS are supplied as solids that have to be first brought into solution, for example, by mineral acid digestion. Depending on the sample and digestion procedure required, the samples would then have to be diluted before analysis – usually between 10 to 100-fold.

During the analytical run however, samples that do not meet the requirements defined by laboratory standard operating procedures (SOPs) may have to be removed from the autosampler rack for additional dilution and subsequent repeat analysis. For example to:

- Confine measured concentrations to within the calibrated concentration range.
- Eliminate the effect of variable, sample dependent matrix suppression of the analytical signal.

While these dilution steps can be manually performed by a skilled laboratory technician it is both tedious and time consuming.



Figure 1. The Thermo Scientific iCAP Q ICP-MS with integrated ESI prepFAST Auto-dilution System.

The ESI prepFAST™ Auto-dilution System in combination with the Thermo Scientific™ Qtegra™ Intelligent Scientific Data Solution™ (ISDS) Software offers the following capabilities for routine trace elemental analysis by the Thermo Scientific™ iCAP™ Q ICP-MS:

- Prescriptive dilution of a single stock standard to generate multiple standards for calibration curves directly from the autosampler rack.
- Per analysis prescriptive dilution of samples directly from the autosampler rack.
- Over calibration range results for samples or QC analyses trigger intelligent, automated dilution to restrict measured concentrations to within a defined range.
- Internal standard recoveries outside of defined limits trigger intelligent, automated dilution to eliminate manual reruns of unexpectedly high matrix samples.

These features allow for fully automated sample preparation and per-analysis data review. Large analysis batches can now be confidently processed without any supervision, freeing up laboratory personnel for other tasks.

prepFAST Operation

The prepFAST Auto-dilution System is based on dual FAST valves operated in combination with a bank of four syringe pumps (S1–S4) that provide improved precision and accuracy over peristaltic pumps. With flow rates of between 1 to 20,000 $\mu\text{L}\cdot\text{min}^{-1}$ the S2 (carrier) and S3 (diluent) syringes can perform dilutions in seconds while the S4 syringe adds internal standard at a constant rate. Speed of dilution is independent of dilution factor (1 to 400) ensuring exact injection timing for all solution regardless of dilution. The operation of the prepFAST is summarised in the 4 steps shown in Figure 2: 1) Vacuum loading of the loop, 2) syringe dilution (S2 & S3) and addition of internal standard (S4), 3) sample injection and 4) loop rinsing (S4).

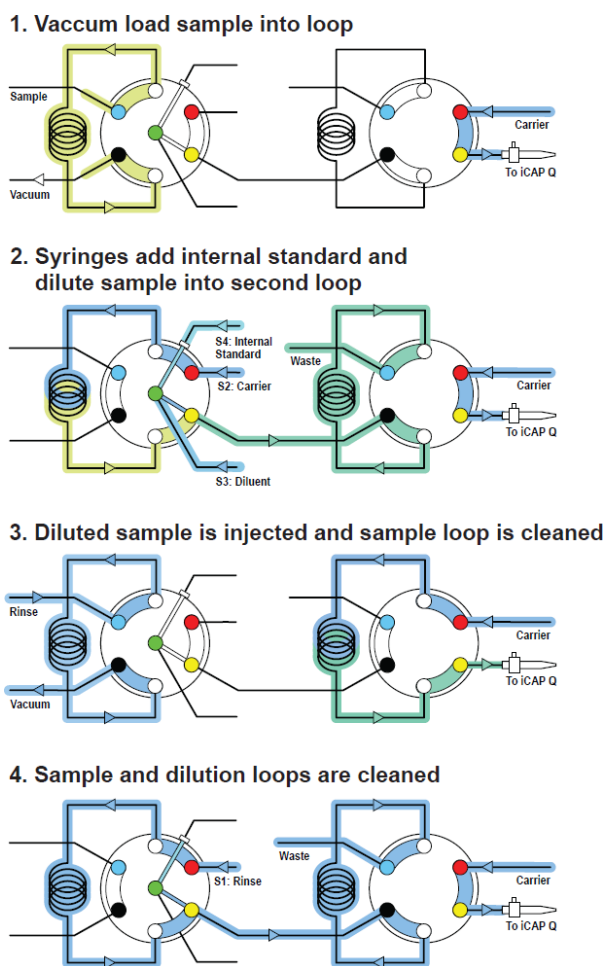


Figure 2. The 4 main steps of prepFAST operation, showing the combination of the 7 and 6-port FAST valves. The prepFAST Auto-dilution System is installed directly beneath the iCAP Q ICP-MS sample introduction system (Figure 1) to provide the shortest sample transfer distance reducing uptake delays to just a few seconds, thereby improving sample throughput.

Since the sample pathway is completely inert problems of cross sample contamination due to the use of peripump tubing are avoided. In the same way prepFAST applications are not limited to aqueous samples but can be applied to organic solvent based samples.

The ESI prepFAST Auto-dilution System provides important advantages for routine analysis with the iCAP Q ICP-MS:

- **High throughput:** Samples are vacuum loaded (~4s) into the prepFAST loop that is mounted directly beneath the sample introduction system. Sample uptake and washout delays are therefore significantly reduced, leading to tangible reductions in complete, sample to sample analysis times.
- **High purity:** Vacuum loading of samples through a fluoropolymer flow path onto the FAST loop is much cleaner than traditional transfer by peristaltic pump tubing, minimizing cross contamination and carry-over.
- **Inline sample preparation:** Internal standard addition and any subsequent dilution is performed inside the valve reducing contamination, enabling high linearity calibration curves for even the lowest concentrations.
- **Automation:** All dilutions are automated, eliminating any errors introduced by manual dilution.
- **Auto-dilution:** Dilution factors of up to 400-fold are reliably and accurately performed with all flows controlled by high precision syringe pumps.
- **Auto-calibration:** Calibration curves with high accuracy and linearity are effortlessly generated direct from a stock standard solution in the autosampler rack.
- **Auto-quality control (QC):** Samples can be individually diluted in position on the autosampler rack without being removed and re-added to/from the rack or analysis queue, eliminating any errors from manual sample handling or data entry.

Software Support of the prepFAST

All aspects of prepFAST Auto-dilution System operation are controlled by a dedicated Qtegra ISDS Software plug-in without having to use any external, secondary software. A series of FAST methods to address common sample handling applications are supplied; all are selectable and editable from within the Qtegra ISDS interface. By fully integrating prepFAST Auto-dilution System into the standard workflow, auto-dilution becomes as easy and routine to use as a standard autosampler.

Automated Calibration

The flexible prescriptive dilution capabilities of the prepFAST Auto-dilution System allow the analyst to choose the appropriate calibration strategy for each application.

- In the simplest approach a single stock standard can be used to create a complete multi-point calibration line (Figure 4).
- For methods that require sample specific calibration ranges (e.g. USP <233>), appropriate standard curves can be generated from a single stock.
- Multiple stocks can be used to create combined calibration curves over extended concentration ranges.
- Separate calibration curves for incompatible elements can be easily created from separate stock solutions.
- Since multiple standard vials are not required, contamination via atmospheric deposition (e.g. B from filters) is minimized.

All of these approaches are possible through the flexible definition of analysis specific prescriptive dilution factors in the Qtegra ISDS Software sample list.

In Figure 3, for example, a 10-point calibration requires a single autosampler rack and vial position, freeing up rack space for additional samples and QC analyses. Note the use of prescriptive dilution factors (prepFAST DF column entries) to define the calibration range.

	Label	Sample Type	Standard	Rack	Vial	prepFAST DF
1	Blank	AVERAGE BLK		3	1	1
2	Blank	AVERAGE BLK		3	1	1
3	Blank	AVERAGE BLK		3	1	1
4	0.010 ppb	STD	4 ppb Stock	3	2	400
5	0.013 ppb	STD	4 ppb Stock	3	2	300
6	0.020 ppb	STD	4 ppb Stock	3	2	200
7	0.040 ppb	STD	4 ppb Stock	3	2	100
8	0.080 ppb	STD	4 ppb Stock	3	2	50
9	0.160 ppb	STD	4 ppb Stock	3	2	25
10	0.4 ppb	STD	4 ppb Stock	3	2	10
11	0.8 ppb	STD	4 ppb Stock	3	2	5
12	2 ppb	STD	4 ppb Stock	3	2	2
13	4 ppb	STD	4 ppb Stock	3	2	1

Figure 3. Generation of a 10-point calibration through the use of prescriptive dilution factors (prepFAST DF column entries) in the Qtegra ISDS Software Sample List.

Figure 4 illustrates the basic approach of generating a 10-point calibration curve. A correlation coefficient of 0.99996 illustrates the dilution accuracy of prepFAST Auto-dilution System at low ng·mL⁻¹ concentrations.

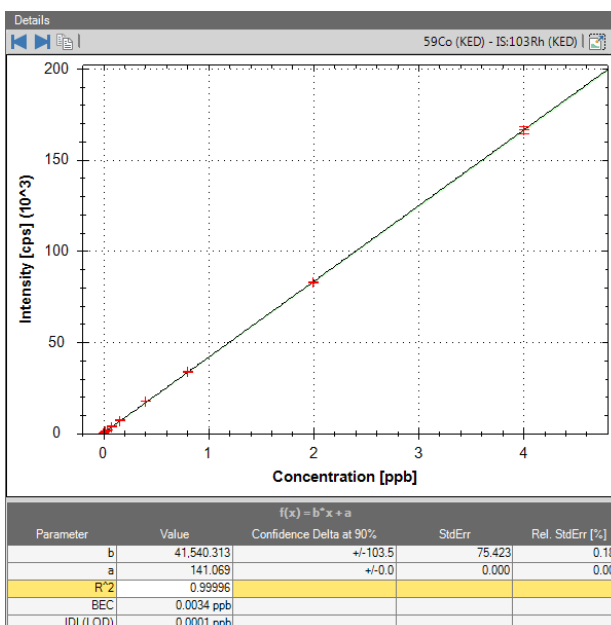


Figure 4. A 10-point calibration generated from a single stock solution using prescriptive dilution.

Automated Sample Dilution

As defined in USP <233> Elemental Impurities – Procedures,¹ all samples have to be diluted “with an appropriate solvent to obtain a final concentration of the Target elements of not more than 2 J” where J is defined by the daily dose of a drug and 2 J is the highest calibration point. To support this sample specific prescriptive dilution factors (prepFAST DF column entries, Figure 3) can be entered in the Qtegra ISDS Sample List (from a text file or LIMS import) and are seamlessly implemented by the prepFAST Auto-dilution System to eliminate manual sample preparation.

Automated Intelligent Dilution

The Thermo Scientific Qtegra ISDS Software supports thirteen separate QC analysis types in addition to any user defined tests. Depending on the protocol defined criteria, Qtegra ISDS can trigger a series of actions in order to address the observed data quality issue. If the QC test requires a new dilution Qtegra automatically inserts a new analysis to the acquisition queue and instructs the prepFAST Auto-dilution System to dilute the sample by an intelligently determined factor.

Over Calibration Range Auto-Dilution

While it is generally considered good laboratory practice to bracket measured concentrations within the calibrated concentration range, this is specifically mandated in some protocols. For example the US EPA states: “Samples with analyte concentrations above the calibration range should have been diluted and reanalyzed.”² While this could be achieved by manual dilution it is often impractical without prior knowledge of the sample and over-range samples have to be manually removed from the autosampler rack, diluted off-line, given a new position in the rack and added again to the analysis queue. Each step in the process is prone to error and potentially costly in terms of materials and time. With Qtegra ISDS Software support of the prepFAST Auto-dilution System however, measured concentrations can be restricted to within the calibration range with intelligent auto-dilution eliminating “reruns.”

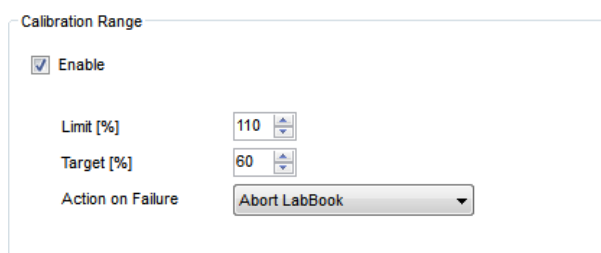


Figure 5. Calibration Range auto-dilution in the Qtegra ISDS Software prepFAST plug-in.

For example, Figure 5 shows how auto-dilution for over calibration range analyses are defined in Qtegra ISDS Software. With the Calibration Range Limit set to 110% (10% above the top standard concentration), any sample or QC analysis with at least one readback value over this limit will be automatically diluted by the prepFAST Auto-dilution System (to give a Target concentration of 60% of the top standard) and reanalyzed.

Internal Standard Range Auto-Dilution

All ICP-MS based instruments suffer from signal suppression when high levels of dissolved solids enter the plasma. Internal standards (IS) are employed in most methods to track signal response. For the analysis of drinking and waste waters, EPA Method 200.8² defines an acceptable IS recovery range of 60–125%.

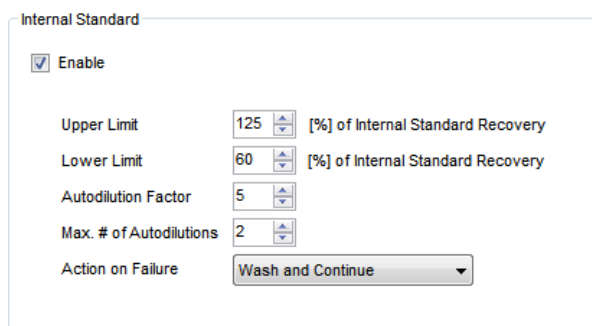


Figure 6. Internal Standard auto-dilution in the Qtegra ISDS Software prepFAST Auto-dilution System plug-in.

Figure 6, for example, shows how auto-dilution for internal standard recoveries are defined in the Thermo Scientific Qtegra ISDS Software. Samples with recoveries outside of the defined range would initially be 5-fold diluted followed by a new 10-fold dilution if required. With routine laboratories facing large numbers of often widely differing samples for 200.8 based analyses, intelligent auto-dilution offers significant throughput improvements.

Conclusion

Automation of the lab workflow has taken a step forward with the integration of auto-dilution. The ESI prepFAST Auto-dilution system has been demonstrated to be a powerful, flexible and robust tool in routine trace elemental analyses by the iCAP Q ICP-MS. The Thermo Scientific Qtegra ISDS based control of the complete system provides a single, simple integrated workflow, eliminating manual dilution in both prescriptive and intelligent, fully automated, analyses. Eliminating manual intervention increases productivity, prevents re-runs and reduces cost of ownership.

References

1. United States Pharmacopeia General Chapter <233> Elemental Impurities – Procedures: Second Supplement to USP 35-NF 30.
2. US EPA – Solutions to Analytical Chemistry Problems with Clean Water Act Methods (EPA-821-R-07-002, March 2007).
3. US EPA Method 200.8 – Determination of Trace Elements in Waters and Wastes by Inductively Coupled Plasma Mass Spectrometry (ICP-MS).

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Netherlands +31 76 579 55 55
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