A Beginner's Guide to ICP-MS

Part IV: The Interface Region

R O B E R T   T H O M A S

The interface region is probably the most critical area of the whole inductively coupled plasma mass spectrometry (ICP-MS) system. It certainly gave the early pioneers of the technique the most problems to overcome. Although we take all the benefits of ICP-MS for granted, the process of taking a liquid sample, generating an aerosol that is suitable for ionization in the plasma, and then sampling a representative number of analyte ions, transporting them through the interface, focusing them via the ion optics into the mass spectrometer, finally ending up with detection and conversion to an electronic signal, are not trivial tasks. Each part of the journey has its own unique problems to overcome but probably the most challenging is the movement of the ions from the plasma to the mass spectrometer. Let's begin by explaining how the ion-sampling process works, which will give readers an insight into the many problems faced by the early researchers.

SAMPLING THE IONS

Figure 1 shows the proximity of the interface region to the rest of the instrument. The role of the interface is to transport the ions efficiently, consistently, and with electrical integrity from the plasma, which is at atmospheric pressure (760 Torr), to the mass spectrometer analyzer region, which is at approximately 10^{-6} Torr. One first achieves this by directing the ions into the interface region. The interface consists of two metallic cones with very small orifices, which are maintained at a vacuum of ~2 Torr with a mechanical roughing pump. After the ions are generated in the plasma, they pass through the first cone, known as the sampler cone, which has an orifice diameter of 0.8–1.2 mm. From there they travel a short distance to the skimmer cone, which is generally sharper than the sampler cone and has a much smaller orifice (0.4–0.8 mm i.d.). Both cones are usually made of nickel, but they can be made of materials such as platinum that are far more tolerant to corrosive liquids. To reduce the effects of the high-temperature plasma on the cones, the interface housing is water-cooled and made from a material that dissipates heat easily, such as copper or aluminum. The ions then emerge from the skimmer cone, where they are directed through the ion optics, and finally are guided into the mass separation device. Figure 2 shows the interface region in greater detail; Figure 3 shows a close-up of the sampler and skimmer cones.

CAPACITIVE COUPLING

This process sounds fairly straightforward but proved very problematic during the early development of ICP-MS because of an undesired electrostatic (capacitive) coupling between the load coil and the plasma discharge, producing a potential difference of 100–200 V. Although this potential is a physical characteristic of all inductively coupled plasma discharges, it is particularly serious in an ICP mass spectrometer because the capacitive coupling creates an electrical discharge between the plasma and the sampler cone. This discharge, commonly called the pinch effect or secondary discharge, shows itself as arcing in the region where the plasma is in contact with the sampler cone (1). This process is shown very simplistically in Figure 4.

If not taken care of, this arcing can cause all kinds of problems, including an increase in doubly charged interfering species, a wide kinetic energy spread of sampled ions, formation of ions gener-
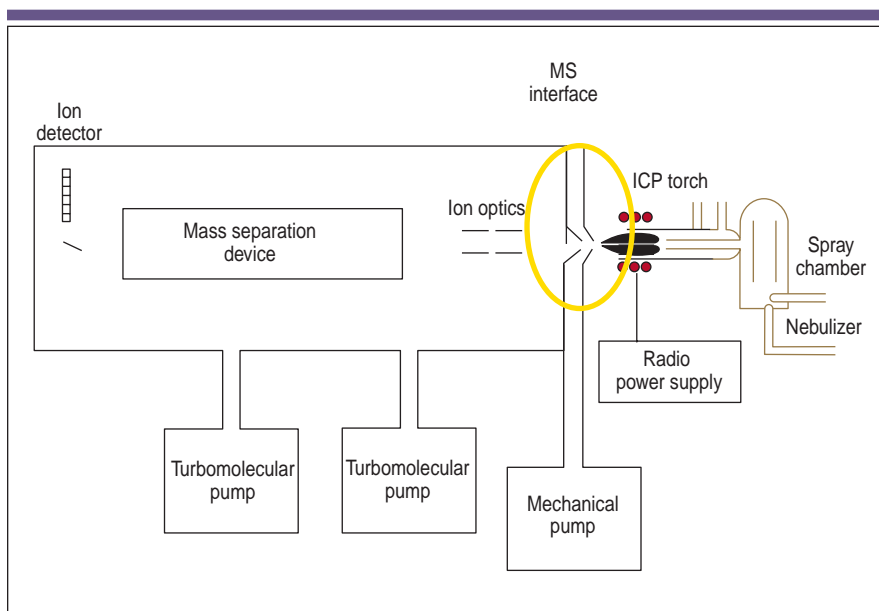

Figure 1. Schematic of an inductively coupled plasma mass spectrometry (ICP-MS) system, showing the proximity of the interface region.
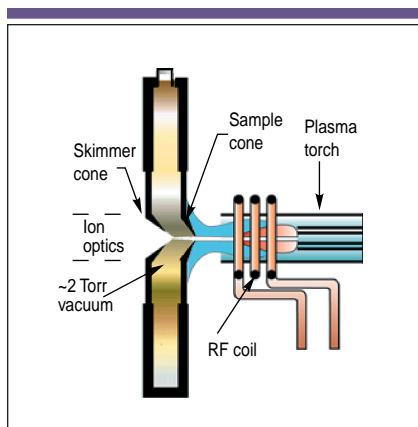
Figure 2. Detailed view of the interface region.

Figure 3. Close-up view of the sampler and skimmer cones. (Courtesy PerkinElmer Instruments, Norwalk, CT.)

Figure 4. Interface area affected by secondary discharge.

ated from the sampler cone, and a decreased orifice lifetime. These problems were reported by many of the early researchers of the technique (2, 3). In fact, because the arcing increased with sampler cone orifice size, the source of the secondary discharge was originally thought to be the result of an electro-gasdynamic effect, which produced an increase in electron density at the orifice (4). After many experiments it was eventually realized that the secondary discharge was a result of electrostatic coupling of the load coil to the plasma. The problem was first eliminated by grounding the induction coil at the center, which had the effect of reducing the radio frequency (RF) potential to a few volts. This effect can be seen in Figure 5, taken from one of the early papers, which shows the reduction in plasma potential as the coil is grounded at different positions (turns) along its length.

Originally, the grounding was implemented by attaching a physical grounding strap from the center turn of the coil to the interface housing. In today's instrumentation the grounding is achieved in a number of different ways, depending on the design of the interface. Some of the most popular designs include balancing the oscillator inside the circuitry of the RF generator (5); positioning a grounded shield or plate between the coil and the plasma torch (6); or using two interlaced coils where the RF fields go in opposing directions (7). They all work differently but achieve a similar result of reducing or eliminating the secondary discharge.

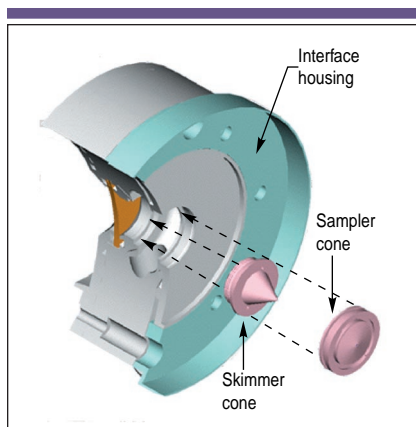## ION KINETIC ENERGY
The impact of a secondary discharge can-

not be overestimated with respect to its effect on the kinetic energy of the ions being sampled. It is well documented that the energy spread of the ions entering the mass spectrometer must be as low as possible to ensure that they can all be focused efficiently and with full electrical integrity by the ion optics and the mass separation device. When the ions emerge from the argon plasma, they will all have different kinetic energies based on their mass-to-change ratio. Their velocities should all be similar because they are controlled by rapid expansion of the bulk plasma, which will be neutral as long as it is maintained at zero potential. As the ion beam passes through the sampler cone into the skimmer cone, expansion will take place, but its composition and integrity will be maintained, assuming the plasma is neutral. This can be seen in Figure 6.

Electrodynamic forces do not play a role as the ions enter the sampler or the skimmer because the distance over which the ions exert an influence on each other (known as the *Debye length*) is small (typically 10^{-3}–10^{-4} mm) compared with the diameter of the orifice (0.5–1.0 mm) (8), as Figure 7 shows.

It is therefore clear that maintaining a neutral plasma is of paramount importance to guarantee electrical integrity of the ion beam as it passes through the interface region. If a secondary discharge is present, it changes the electrical characteristics of the plasma, which will affect the kinetic energy of the ions differently, depending on their mass. If the plasma is at zero potential, the ion energy spread is in the order of 5–10 eV. However, if a secondary discharge is present, it results in a much wider spread of ion energies en-
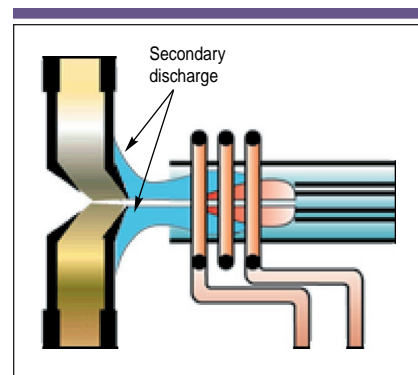
tering the mass spectrometer (typically 20–40 eV), which makes ion focusing far more complicated (8).

BENEFITS OF A WELL-DESIGNED INTERFACE
The benefits of a well-designed interface are not readily obvious if simple aqueous samples are analyzed using only one set of operating conditions. However, it becomes more apparent when many different sample types are being analyzed, requiring different operating parameters. A true test of the design of the interface occurs when plasma conditions need to be changed, when the sample matrix changes, or when a dry sample aerosol is being introduced into the ICP-MS. Analytical scenarios like these have the potential to induce a secondary discharge, change the kinetic energy of the ions entering the mass spectrometer, and affect the tuning of the ion optics. It is therefore
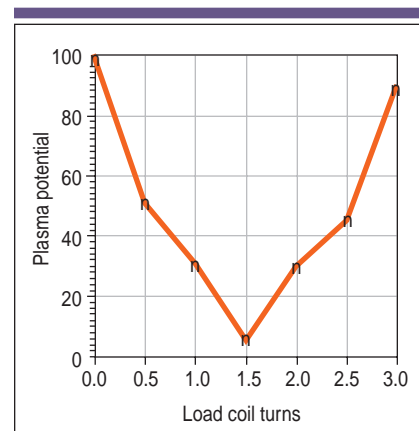

Figure 5. Reduction in plasma potential as the load coil is grounded at different positions (turns) along its length.
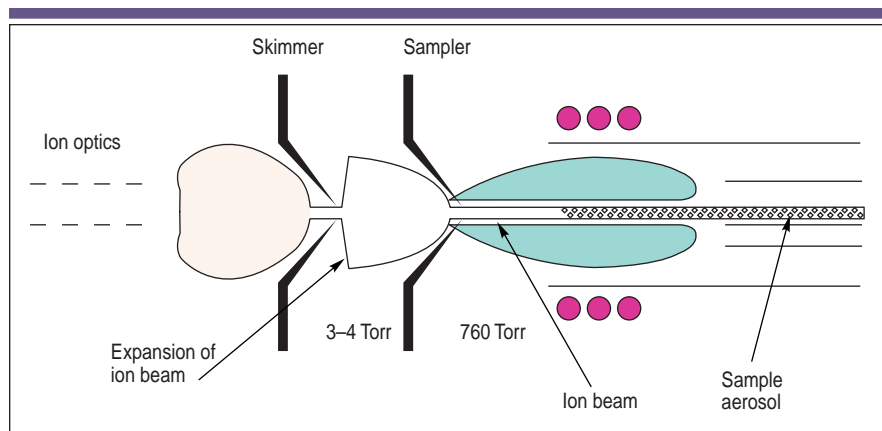
Figure 6. The composition of the ion beam is maintained, assuming a neutral plasma.

Figure 7. Electrodynamic forces do not affect the composition of the ion beam entering the sampler or the skimmer cone.

critical that the interface grounding mechanism can handle these types of real-world applications, of which typical examples include
• The use of cool-plasma conditions. It is standard practice today to use cool-plasma conditions (500–700 W power and 1.0–1.3 L/min nebulizer gas flow) to lower the plasma temperature and reduce argon-based polyatomic interferences

such as $^{40}Ar^{16}O$, ^{40}Ar, and ^{38}ArH, in the determination of difficult elements like ^{56}Fe, ^{40}Ca, and ^{39}K. Such dramatic changes from normal operating conditions (1000 W, 0.8 L/min) will affect the electrical characteristics of the plasma.
• Running volatile organic solvents. Analyzing oil or organic-based samples requires a chilled spray chamber (typically −20 °C) or a membrane desolvation sys-
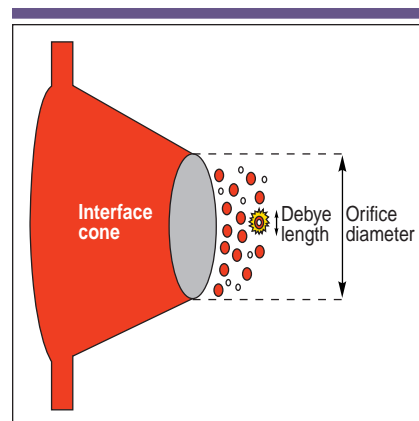
tem to reduce the solvent loading on the plasma. In addition, higher RF power (1300–1500 W) and lower nebulizer gas flow (0.4–0.8 L/min) are required to dissociate the organic components in the sample. A reduction in the amount of solvent entering the plasma combined with higher power and lower nebulizer gas flow translate into a hotter plasma and a change in its ionization mechanism.
• Reducing oxides. The formation of oxide species can be problematic in some sample types. For example, in geochemical applications it is quite common to sacrifice sensitivity by lowering the nebulizer gas flow and increasing the RF power to reduce the formation of rare earth oxides, which can interfere spectrally with the determination of other analytes. Unfortunately these conditions have the potential to induce a secondary discharge.
• Running a "dry" plasma. Sampling accessories such as membrane desolvators, laser ablation systems, and electrothermal vaporization devices are being used more routinely to enhance the flexibility of ICP-MS. The major difference between these sampling devices and a conventional liquid sample introduction system, is that they generate a "dry" sample aerosol, which requires totally different operating conditions compared with a conventional "wet" plasma. An aerosol containing no solvent can have a dramatic effect on the ionization conditions in the plasma.

Even though most modern ICP-MS interfaces have been designed to minimize the effects of the secondary discharge, it

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Validation of Spectrometry Software

Part II: Roles of the Validation Plan and User Requirements Specification

R.D. McDowall

I n this month's column we will explore why the user requirements specification (URS) and the validation plan are so important for the validation of spectrometry software, and we'll cover the specification and system selection from a software perspective.

In the first installment of this series, we looked at the system development life cycle (SDLC) and some validation concepts (1). One concept was that validation is a process that covers the entire system development life cycle: Once started, you can't stop. Now we will look in more detail at the first part of the SDLC.

THE WAY IT WAS

In the past, the spectrometer and software were purchased and then, just before they were put into operational use, someone thought about validation. Some common questions may have been

- Have we validated the system? No.
- Does it matter? Probably.
- Will we get caught? Don't even think about answering no to this question.

Considering validation at such a late stage of the life cycle will mean a delay in

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going operational, thus failing to gain benefit from the investment in the instrument or going live with no regulatory coverage. It depends on your approach to risk and if can you sleep at night.

THE WAY IT SHOULD BE

However, as we discussed in the previous article in this series, a proactive approach to validation is necessary and, if done right, will actually save you money by ensuring that you buy the right instrument for the job. So we'll start at the beginning and look at the first stages of the life cycle:

- Defining and controlling the validation throughout the whole life cycle (writing the validation plan).
- Specifying what you want the system to do (writing a user requirements specification).
- Selecting the system using the requirements defined in the URS as the basis, rather than "the salesperson bought me a good meal."

Defining and controlling the overall validation. The validation plan is one name for the document that controls the validation effort for your spectrometer software. However, the name for this document varies from laboratory to laboratory. It may be called the validation plan, master validation plan, validation master plan, or quality plan.

Regardless of what you call this document in your organization, it should cover all the steps you are going to take to demonstrate the quality of the spectrometry software in your laboratory.

Ideally the validation plan should be written as early as possible in the life cycle to define the overall steps that are required as well as the documents to be produced during each phase of the life cycle. There are different approaches to writing validation plans, and the document can be written in several stages in the life cycle.

I'll outline my philosophy and rationale now and you, dear reader, can accept this as is, modify it, or ignore it.

First, you should write the validation plan as either the first or second document in the life cycle; I advise writing it after the first or second draft of the URS to incorporate any implementation or roll-out issues in the overall validation strategy. The rationale for this approach is that the validation plan provides documented evidence of intent of the validation. The document will set out the overall strategy of the validation and define the life cycle phases and the documented evidence that will be produced in each phase. If you leave writing the validation plan until later in the project, one or more phases of the life cycle will have passed and you may need to write documents retrospectively. Furthermore, you'll be out of compliance with *21 CFR 11.10(k)(2)*, which requires a time-sequenced audit trail of systems documentation.

Content of a validation plan. The purpose of a validation plan is to provide documentation of intent for the whole validation, including a definition of the life cycle used, documentation to be produced during the each stage of the life cycle, and roles and responsibilities of everyone involved in the project.

To provide a better perspective, the content of a validation plan is listed in the sidebar. It is based on the Institute of Electronic and Electrical Engineers (IEEE) standard for validation and verification plans (2).

This document is important because it defines what you will do in the validation, and you will be judged against it when your operation is inspected. Therefore, read and understand it well — don't write the plan and forget it, because what you plan does not always come to pass. Usually deviations from the plan occur that

you'll need to record, such as documents not written, new documents required that have not been specified, or parts of the life cycle omitted or modified. These changes will need to be noted under the deviation procedure that you have in place in the plan. Noting the changes sounds like a pain, but once the principles are understood, it is relatively simple to do.

DESIGN: THE URS

How much money have you wasted on purchasing spectrometers that were not fit for purpose, did not do the job you wanted, or used software that was not up to snuff? From a business perspective, a document that says what you want the instrument and software to do will be beneficial, because you'll have a better chance of selecting the right instrument and software.

From a regulatory perspective, remember that the definition of validation presented in the first part of this series (1) included that phrase "predefined specifications." The document that provides the laboratory with the predefined specifications for the spectrometer and the software is the URS. Without this document or an equivalent, you cannot validate your spectrometer software, because you don't have a predefined specification and therefore there is nothing to test against. This is particularly important when you consider which electronic record and electronic signature functions are pertinent to define and test for the way that you will use the instrument.

The URS provides the answer to the question, What do you want the system to do? This makes the assumption that you know what you want the system to do.

A well-written URS provides several specific benefits. For one thing, it serves as a reference against which off-the-shelf commercial products are selected and evaluated in detail and any enhancements are defined. Also, you are less likely to be seduced by technology or buy a poor system. Furthermore, the URS reduces the total system effort and costs, because careful review of the document should re-

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Validation Plan Outline Format Based on IEEE Std. 1012-1986

Purpose
What is the scope of the validation: What is the spectrometry system to be validated?

Reference documents
Include references to any regulations, documents, guidelines, or internal policies and procedures that affect the validation of this spectrometer.

Definitions
Define key words and terms.

Validation overview
Define the roles and responsibilities for the validation, and include both internal and external people involved. Meaning of signatures: Why are you signing a document? Cross-reference to the project plan for the schedule of work. (This should be a separate document and can be updated as the validation progresses — or not, as the case may be.)

Life cycle validation
Define the system development life cycle that you'll be using for the validation. For each phase, state what the activities will be and what documented evidence you will be producing. Don't forget: some of this may be electronic, especially during the qualification phases.

Validation reporting
Outline how the validation will be reported.

Validation administration procedures
State how change control for deviations, software bugs, and so forth will be handled. The validation plan is a controlled document, so it must be paginated correctly (for example, page X of Y), signed by the author, authorized by two others (technical and compliance/release reviews), and distributed to specified individuals.

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veal omissions, misunderstandings, and inconsistencies in the specification. This means that they can be corrected easily before you purchase the system. Finally, a well-written URS provides the input to user acceptance test specifications and qualification of the system.

General guidelines for a URS. A user requirements specification clearly and precisely defines what the customer (that is, you) wants the system to do, and it should be understood by both the customer and the instrument vendor. The URS is a living document and must be updated, via a change control procedure, throughout the computer system life cycle. After purchase, when you upgrade the software, also update the URS to reflect the changes and new functions in the latest version.

A URS defines the functions to be carried out, the data on which the system will operate, and the operating environ-

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ment. Ideally, the emphasis is on the required functions and not the method of implementation, as this may be the identification of a solution. The aim of a URS is to make a statement of requirements rather than a statement of a potential solution. This allows users to look objectively at software from different vendors and make an objective decision as to which system is required.

Nature of the URS. The URS should address the following basic issues:
• Functionality: What is the system or function supposed to do?
• External interfaces: How does the system interact with other systems and the users?
• Performance: What are the speed, availability, and response time of the various functions of the system?
• Attributes: What are the security considerations of each function?
• Design constraints: Must the system work on specific hardware or use an operating system, and are these consistent with your organization's standards?
• Prioritization: All requirements are ranked for importance as either mandatory or desirable (respectively, you must use the system, or it would simply be nice to have it).

The URS should form the basis of the solution to be delivered by the selected vendor. If this does not happen, you can leave yourself open to a poor-quality product because either you don't know what you want the system to do or you can't articulate this need to the vendor.

Writing the specification. The following guidelines should be followed during the production of the specification:
• Each requirement statement should be uniquely referenced and no longer than 250 words.
• The URS should be consistent; therefore, requirement statements should not be duplicated or contradicted.
• The URS should express requirements and not design solutions.
• Each requirement should be testable (this allows the tests to be designed as soon as the URS is finalized).

Table I: Example Specification of Audit Trail Requirements for Spectrometer Software

Requirement Number	Spectrometer Data System Feature Specification	Priority (M/D)*
5.1.01	The system software requires an audit trail to monitor the creation, modification and deletion of all electronic records generated and managed by the system.	M
5.1.02	The audit trail covers all acquisition, control, calibration, calculation, display, reporting, and export functions and includes all file handling options such as open, copy, edit, rename, and delete.	M
5.1.03	The audit trail is able to support the system during normal operation without an excessive system overhead or loss of performance.	D
5.1.04	The audit trail once invoked cannot be switched off.	M
5.1.05	Archival of electronic records will have an audit trail entry.	M
5.1.06	Selected portions of the audit trail must be made available either by printing or viewing. These partial audit trail reports must be made available in a portable electronic format for use by regulatory agencies.	D
5.1.07	The audit trails must be maintained for as long as the electronic records they correspond to exist.	M
5.1.08	When a record is changed, all previous versions must be readable or available for inspection.	M

*Mandatory or desirable

- Both customer and vendor must understand the document; therefore, jargon should be avoided, and key words should be defined in a specific section in the document.
- Requirements should be prioritized as mandatory or desirable.
- The URS should be modifiable, but changes should be made under a formal control procedure.

A URS is correct if every requirement stated has only one interpretation and is met by the system. Unfortunately, this is rare.

Organizing requirements: Go with the workflow. A URS can be extensive unless you plan well, so careful consideration should be given to organizing requirements in the easiest manner to understand. The best framework for writing a user requirements specification for most spectrometers is to follow the process or workflow that the data system will be automating. Therefore, if you have mapped the process, it makes an ideal prompt for the URS because the requirements can be defined against each activity in the process.

This idea of documenting what we want in sufficient detail sounds great, but it means more work, doesn't it? Yes, that is true, but consider the benefits. The more time you spend in the specification and design phase getting your ideas and concepts right, the quicker the rest of the life cycle will go if you know what you want. You will get a spectrometer and associated software that meet your requirements more fully, and there will be less chance later in the life cycle of finding out that what looked good early on does not meet certain key requirements now.

Contrast this to selecting a spectrometer with no user requirements. (This bit should be easy, because we have all done it.)

Don't forget the instrument specs! In this series we'll concentrate on the software elements, but don't forget the instrument itself. The software and the instrument must be an integrated system. So, the instrument specification also needs to be included in the overall URS. What operating requirements do you need from the spectrometer, such as mass range and resolution or wavelength? Get them down in the URS.

A specific example. Table I shows an example of what a URS could look like. It defines the requirements for audit trail functionality in the spectrometer software to meet Part 11 requirements. Looks impressive, doesn't it? Look at the table and you'll see that each requirement is

uniquely numbered (not bad), short (good), and prioritized (getting better). However, *21 CFR 11* states that every change must not overwrite the original result and must include the name of the user, along with date and time of the change. This is not mentioned in this specification (bummer!). So be careful, specify the system, and review it carefully or something essential may be missed.

SYSTEM SELECTION: PART ONE
Because your requirements for the overall system are contained in the URS, the document can be used as a basis to design the tests to evaluate the various systems offered by vendors. Can the systems offered meet your requirements, especially for the mandatory functions? Using the URS requirements for system selection helps ensure that the system selected matches your business needs.

Don't forget that the tests you use for system selection should also include common problems that you know happen in your laboratory. What happens when samples are switched and you notice the error only after the analysis? Can the system handle the changes easily and with suitable audit trail entries?

The system you select will be based on the practical experience of using it in your laboratory environment. However, before you sign on the dotted line, you may want to make sure that the software was developed in a quality manner through a vendor audit.

VENDOR CERTIFICATES AND AUDITS
Many spectrometer vendors will be certified to ISO 9000 of some description and will offer you a certificate that the system conforms to its quality processes. This is fine, but please remember that no requirement for product quality exists in any ISO 9000 schedule, and if you look at the warranty of any software product, there is no guarantee that the software is stated to be either fit for purpose or error free. The certificates are fine, but if the system is critical to your operation, my advice is to consider a vendor audit.

The vendor audit should take place once the product has been selected. The purpose is simply to see if the ISO 9000 quality system is operated effectively. The evaluation and audit process is a very important part of the life cycle, because it shows whether design, building, and testing stages (which are under the control

of the vendor) have been checked to ensure compliance with the regulations. The audit should be planned and should cover items such as the design and programming phases, product testing and release, documentation, and support; a report of the audit should be produced after the visit. Two published articles have covered vendor audits in more detail (3, 4).

The minimum audit is a remote vendor audit using a checklist that the vendor completes and returns to you. This is usually easy to complete, but the writer of the checklist must ensure that the questions are written in a way that can be understood by the recipient, because language and cultural issues could affect a remote checklist. Moreover, there is little way of checking the answers you receive. However, for smaller software systems — and some spectrometers fall into this category — a remote audit is a cost-effective way of getting information on how a vendor carries out its development process, so long as you know and understand its limitations.

SYSTEM SELECTION: PART TWO

If the vendor audit, price quote, instrument, and software are all acceptable, you'll be raising a capital expenditure request (or whatever it is called in your organization) and then generating a purchase order. The quote and the purchase order are a link in the validation chain; they provide a link into the next phase of the validation life cycle: qualification. The purchase order is the first stage in defining the initial configuration of the system, as we'll discover in the next article in this series.

REFERENCES
(1) R.D. McDowall, *Spectroscopy* **16**(2), 32–43 (2001).
(2) IEEE Standard 1012-1986, "Software Validation and Verification Plans," Institute of Electronic and Electrical Engineers, Piscataway, NJ, USA.
(3) R.D. McDowall, *Sci. Data Mgmt.* **2**(2), 8 (1998).
(4) R.D. McDowall, *Sci. Data Mgmt.* **2**(3), 8 (1998). ◆

shouldn't be taken for granted that they can all handle changes in operating conditions and matrix components with the same amount of ease. The most noticeable problems that have been reported include spectral peaks of the cone material appearing in the blank (9); erosion or discoloration of the sampling cones; widely different optimum plasma conditions for different masses (10); and increased frequency of tuning the ion optics (8). Of all these, probably the most inconvenient problem is regular optimization of the lens voltages, because slight changes in plasma conditions can produce significant changes in ion energies, which require regular retuning of the ion optics. Even though most instruments have computer-controlled ion optics, it becomes another variable that must be optimized. This isn't a major problem but might be considered an inconvenience for a high–sample throughput lab. There is no question that the plasma discharge, interface region, and ion optics all have to be designed in concert to ensure that the instrument can handle a wide range of operating conditions and sample types. The role of the ion optics will be discussed in greater detail in the next installment of this series.

REFERENCES
(1) A.L. Gray and A.R. Date, *Analyst* **108**, 1033 (1983).
(2) R.S. Houk, V. A. Fassel, and H.J. Svec, *Dynamic Mass Spectrosc.* **6**, 234 (1981).
(3) A.R. Date and A.L. Gray, *Analyst* **106**, 1255 (1981).
(4) A.L. Gray and A.R. Date, *Dynamic Mass Spectrosc.* **6**, 252 (1981).
(5) S.D. Tanner, *J. Anal. At. Spectrom.* **10**, 905 (1995).
(6) K. Sakata and K. Kawabata, *Spectrochim. Acta* **49B**, 1027 (1994).
(7) S. Georgitus, M. Plantz, poster paper presented at the Winter Conference on Plasma Spectrochemistry, FP4, Fort Lauderdale, FL (1996).
(8) D.J. Douglas and J.B. French, *Spectrochim. Acta* **41B**, 3, 197 (1986).
(9) D.J. Douglas, *Can. J. Spectrosc.* **34**, 2 (1089).
(10) J.E. Fulford and D.J. Douglas, *Appl. Spectrosc.* **40**, 7 (1986).

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