Technical Note

Validation of Methods in ICP OES - Keys to Success Using a Total Solution

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1 Introduction

Today, laboratories are confronted with the challenges of better quality assurance and certification. One of the main routes to good quality is validation of methods. Validation is the procedure that allows you to verify that the analytical method used does what it is supposed to do both in terms of the results and the suitability of the instrument to a given analytical problem.

Further, some industries have issued stringent regulations for both the methods and instrumentation. One such regulation is the pharmaceutical industries FDA 21 CFR Part 11 dealing with electronic records and signatures.

2 Stages of Validation

One can differentiate different stages in the process of validation. We are going to explain below some of these stages.

2.1 Analytical problem

To define an analytical problem, it is necessary to specify the quality required for the analytical results (accuracy and repeatability), and those required for the instrument (limits of detection, quantification and robustness) with thresholds of the acceptance limits. It is necessary to know whether the instrument can determine the limits of detection required, perform accurate quantification with different matrices, long-term stability, etc.

2.2 Characteristics of the sample

It is evident that an analytical method is developed for a particular type of sample. Regrettably, we do not always know the samples that should be analyzed.

2.3 Certified reference material (CRM)

A CRM is a material where the element concentrations are known with inter-laboratory analysis showing the data uncertainty and traceability. The CRM has a guarantee when accompanied by a certificate. On this certificate it states the procedure and establishes the mean concentration with the variation and individual laboratory results. Every guaranteed value is accompanied with an uncertainty at an indicated reliability level.

2.4 Necessary materials

Any material needed must be specified: water, reagents, flasks, crucibles, means of heating (dry block, hotplate).

2.5 Instrument tests

Regular tests must be performed to verify the proper functioning of the instrument. JY suggests using a diagnostic method as described in Application Note 3 and Technical Note 16. The experiments described are fast and easy to conduct and can be stored as a standard analytical method. The results of the experiments can provide some explanation about the origin of a degradation of the analytical performance. These experiments can also be easily adapted to set up control charts, once the accepted values of the line intensities and ratios and their fluctuations have been determined.

2.6 Analytical methods

The measurement parameters used in the analysis must be clearly defined and justified: choice

of lines, peak mode, type and positions of background corrections, parameters of the spectrometer, number of replicates, calculation mode, calibration procedure, internal standard, etc.

2.7 Electronic records

An electronic record "is any combination of text, graphics, data, audio, pictorial, or other information represented in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system".

For an ICP OES instrument electronic records include method parameters, calibration data, original data, processed data and analysis reports.

2.8 Interpretation of results

The interpretation of results includes:
1. Calculation of the limits of detection and quantification,
2. Study of the linearity of the calibration curves (e.g., by analysis of variance),
3. An accuracy check with a reference material or method of standard additions,
4. The evaluation of standard deviation (10 replicates are necessary for good statistical estimation).

2.9 Uncertainty

The analyst has to give a concentration in the form: value ± uncertainty. The calculation of uncertainty is very delicate: it includes known uncertainties (flasks) and estimated uncertainties (succession of at least 10 measurements under identical conditions). The measurement uncertainty is then the combination of different standard deviations such as preparation of the sample, the flask, operator effect, calibration and the pipette.

2.10 Revalidation

It is necessary to define the frequency of revalidation as well as the procedure of revalidation.

2.11 Inter-laboratory validation

Participation in inter-laboratory exercises is essential to discover systematic errors such as effects of the the matrix, poor sample preparation, etc.

3 Analyst™ ICP software and electronic records

There are many advantages of using electronic records compared to paper records. For example, the storage space required is much lower. Additionally, computers are already used for the acquisition of data and for analysis, so allowing only electronic records to be stored increases productivity and gives faster access to these records. In order to allow the use of electronic records and to maintain data integrity the industry requested a regulation covering the topic be issued. In response, the FDA issued Rule 21 CFR-Part 11 in 1997 to formally set requirements for the use of computers, electronic records and electronic signatures. This rule applies to all industry sectors that are regulated by the FDA including those that conform to Good Laboratory Practice (GLP), Good Clinical Practice (GCP) and current Good Manufacturing Practice (cGMP).

This ruling has a significant impact for those using analytical instrumentation with many changes in the way data is acquired and treated. For example, providers may have to be developed to determine who has authorized access to the electronic records and who has the authority to edit then. The computer associated with the instrument, and its software, are critical in conforming to this ruling.

Below are the primary requirements for the analytical laboratory to conform to the 21-CFR-Part 11 rule and the JY Analyst™ ICP software's ability to meet these requirements.

- Use of validated existing and new equipment and computer systems

JY offers validation services and documentation for all JY ICP spectrometers.

- Secure retention of electronic records to instantly reconstruct the analysis

Analyst™ software retains an un-editable report of the analysis, including conditions, calibration data, and analysis data. This data contains enough information to reconstruct the analysis.

- User independent computer generated time-stamped audit trails

Each step of an analysis is time stamped by the computer.

- System and data security, data integrity and confidentiality through limited authorized system access

Analyst™ software can be set for password access. In this case, the data cannot be edited or viewed without using a login and password. Different users can be given different levels of access to the software. Thus, this provides the required system and data security, data integrity and confidentiality.

- Use of secure electronic signatures for closed and open signatures

Analyst™ software login and password can be used as an electronic signature, as defined by the FDA. The name of the user undertaking an analysis will be stored along with the data.

4 Conclusion

Understanding the validation process and having compliant software is only the first step for users to achieve success. Users must have appropriate training and standard operating procedures (SOP). For example, meeting the requirements for 21-CFR-Part 11 is only part of the solution for a pharmaceutical analytical laboratory. The analytical equipment must routinely perform to the requirements. JY offers a family of ICP spectrometers featuring high performance and fast, accurate results in a reliable, proven platform. In addition, training programs are offered to educate users of all levels on the operation and use of both instrument and software.

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