

VALIDATION

An analytical method is the procedure for determining the “characteristics” of a material. These characteristics can be physical, such as melting point or density, or chemical, such as the amount of a particular chemical in a material. The analytical method is the detailed set of directions, from the preparation of the test sample to the reporting of the results. This protocol must be followed exactly for the results to be accepted for the stated purpose.

The goal of any analytical method, whether for measuring pesticides in food, an active ingredient in a pharmaceutical product, or a marker compound in a botanical raw material, is to provide accurate, reproducible results. How do we know that a method yields accurate, reproducible results? By performing a systematic series of experiments on the method to determine certain “performance characteristics.” The process of determining these performance characteristics is called “validation.”

Many people use the term “validated method” or “validation” very freely without really understanding what the term means. Strictly speaking, method validation is a systematic and well-defined process of demonstrating or confirming the “performance characteristics” of an analytical method. The key “performance characteristics” are the accuracy (how close the results obtained by a particular method are to the true or real value) and the precision (what kind of variability can be expected in the results when the analysis is repeated). Simply put, validation is demonstrating that the method is suitable for its intended purpose. A method validated for use with one material or product may not be valid for use on another material or product. The responsibility of proving that a method works with a particular material or product lies squarely with the user of the method.

It is important to realize that there are different levels of validation. The most basic level of validation occurs in a single laboratory, and is called, appropriately enough, “single laboratory validation,” or SLV for short. An SLV is a series of experiments that demonstrates the performance characteristics of a method in a particular laboratory, but it gives no information about how reproducible the results of the method will be when it is used in another laboratory. The SLV study is also the means by which a laboratory may prove that a method is suitable for the analysis of a particular product or ingredient in their own laboratory.

When a few labs participate in the validation, we can get an idea about how reproducible the results of a method are, and this type of validation is often referred to as a “peer verified” validation.

If at least 8 laboratories participate in a validation study, we can then get a very good estimate about the reproducibility of the method, and at this point it becomes known as a “collaboratively studied” method. All AOAC Official Methods of Analyses must successfully complete a collaborative study.

Method validation, especially at the single-laboratory level, is usually a time consuming and costly process. Even under the best of circumstances, validating a method for a single analyte in a single material could take a couple of weeks. Since there are several thousand different ingredients in commerce in the dietary supplement industry, and since a significant portion of

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these ingredients may need multiple methods, the chances of any laboratory having validated methods for all of those ingredients are practically non-existent.

In practice, laboratories can generate validation data on new methods or existing methods being used on new materials concurrently with real-time analyses. By using multi-point calibration curves, performing replicate test preparations, and using one or more control materials each time a method is run, linearity and precision data can be generated over time, and often provides much more reliable information about a method's performance than when an entire validation is performed at once.

There are a number of guidelines for validating methods in-house, including AOAC International, the United States Pharmacopeia, ISO/IEC, Eurochem, and the International Conference on Harmonization (ICH), among others. Although all these organizations have similar guidelines, there are some differences, and some (particularly AOAC I) provide much more detail than others. Depending on your specific validation needs, one or more of the guidelines may be useful.

