



A Guide to Hemp Method Validations

Paper Four — Five Part Series

Executive Summary

Validation studies can be described as either internal or external. This paper will go over the differences between these two ways to validate a method and list the various benefits of internal and external method validations.

Understanding Internal vs. External Validation

In order to evaluate a method, its performance should be characterized within a validation study. The study should clearly outline the experimental conditions to be evaluated, any equipment required to perform the analysis, and identify the intended scope of the method. As previously discussed, specific studies (matrix testing, selectivity, LOD, robustness)¹ are needed to validate a method. These studies are complex and require advanced training and knowledge to perform. As a result, the validation studies are typically performed in one of two settings: within the method developer's laboratory (internal validation) or at a third-party laboratory (external validation). There are advantages to each of these types of validation, and depending on the intended market of the assay, one type may be more beneficial than the other. This paper will explore the differences between internal and external validation studies and provide details on the advantages of each type.

Highlights of Internal Method Validation

As consumers, products that have been independently evaluated will often be perceived as more desirable than their competitors. The prevailing thought is that independently collected data is superior to internal data, but is that always the case? While external validation studies may offer some advantages, internally validated methods often provide a more robust understanding of the performance of a method.

- Increased scope of application — Method data collected during an internal validation can be less expensive to obtain than when performed by external laboratories. That can provide a method developer a larger budget to expand the scope of applicability of the assay. Expanded scopes are advantageous to end users. The more matrices included in the scope, the easier it is for end users to onboard the method as it reduces the volume of verification testing required.
- Method optimization — Internal validation studies offer the benefit of the continued evaluation of testing protocols. Testing can be performed using a single or factorial robustness type study to determine optimal conditions for detection or quantitation.
- Flexibility — An internally validated method can be designed to go beyond traditional validation guidelines. Studies can be built to integrate more variability, exploring different lots or brands of media, reagents, and supplies, or incorporating multiple operators or instrumentation into the analysis into the method's performance. Having access to this data will supplement the overall statistical data obtained during the validation. This information can be useful to end users who may source materials from multiple vendors or who may be hesitant to onboard technology based on the skill level of their team.
- Trustworthy data — When testing at third-party laboratories, the operators performing the method are often not as fully trained on performing the method as the technicians of the method developer. This can lead to results that may be viewed as less than ideal but result from a lack of experience with the method more than can be attributed to the method's performance. When performed internally by individuals with knowledge of the method, the data collected can be considered a best case scenario and provide more clear insight into the method's performance.
- Independent evaluation is still possible — Internal validation study can also include independent evaluation. Methods are often developed within R&D departments, which may be separate from a validation department, and allows for independence in the validation study. Alternatively, the use of blind coded replicates or using analysts not involved in developing the method can provide the same independent evaluation.
- Internally validated methods still follow standardized validation guidelines. This allows you, as an informed end user, the power to evaluate the data independently to understand if the method is the right fit for you!





Benefits of an External Validation

For some methods, technology providers may decide to engage in external validation studies. This type of validation may occur through a third-party certification organization or may be a third-party validation organized by the method developer. In either case, external validation studies are performed to verify the work performed during internal validation. The objective is to make sure that the method works outside of the expertise of the method developer in the hands of end users. External validation provides unique values in some areas that are not always able to be achieved internally.

- Independent evaluation — An external validation study, by its name, will require an evaluation of the method by a group that is not the method developer. This type of testing provides end users assurance that the method performed sufficiently in similar situations to those in which they may use it. Independent evaluations can be performed by expert labs as part of a certification process or by industry/contract laboratories to evaluate the method's performance.
- Certification — A common objective of external validation studies is to allow certification of the method by a third-party organization. These organizations (AOAC, Health Canada, NCIMS) require independent analysis of the method as part of their conformity assessment programs, so an external validation study is mandated. Method developers can use this requirement as an opportunity for external validation to serve as part of the certification of the method.
- Regulatory acceptance — One of the main objectives of the third-party certification process is to gain regulatory acceptance of the method within a given industry. While not all industries require certification, those who do will not allow methods to be used until they have achieved this status. An external validation study can meet this requirement.
- Peer review process — Data generated from external studies is often combined with internal validation data and submitted as part of a peer review process. This is required for most third-party certification organizations, although method developers will often explore this option and the publication of the data in a scientific journal (JFP, JAOAC) as part of an internal validation study as well.
- Standardized studies — External studies will often follow strict study designs. These studies are designed to evaluate a method, not determine optimization conditions. Because of this, data generated from one external study is more easily compared to that of another method, providing end users with comparable data in determining which method they prefer to use.

Conclusion

Internal and external validations should both be considered when validating an assay. Depending on the intended market, each can provide unique benefits to the end product. Internal validations provide the flexibility to optimize testing protocols during the validation process and can still incorporate an independent component when a separate validation laboratory within the company is utilized. Alternatively, external validations allow for completely independent evaluation and often result in various third-party certifications and regulatory acceptance.

1 See Paper 2: *What does it mean to have a validated method* and Paper 3: *Differences in Validation Requirements for Microbiology, Chemistry or Allergens*