



SLV

(Single Laboratory Validation)

A Key Step Along The Path To

OMA

(Official Methods of Analysis)

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Today's Takeaways



- **Learn About The AOAC Validation Process**
- **Focus On Quantitative Chemical Methods**
- **Identify Key Aspects Of The Validation Process**
- **Discuss Efforts To Harmonize AOAC Processes**
- **Why Method Optimization Is Needed**
- **Benefits Of Performing An SLV**
- **What Next? – How To Use The AOAC Process**



Overview of the New Process



- **Communities, Stakeholders, or a Company Identify a Problem that can be Solved by a Method Action**
 - They come together with facilitation
 - Recognize and define needs, goals & possible funding sources
 - Select experts for technical review & decision making
 - Select candidate methods for review/optimization/validation
 - Select a Study Director to perform a Single Lab Validation
- **Submit an application to AOAC International**
 - AOACI makes sure all items are present & steps are followed

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Request for Review Appointments



- **Expert Review Panel(s)**
- **Community Chair/Voting Member(s)**
- **Community Task Group(s)**
- **Stakeholder Panel(s)**
- **Other (to be specified)**

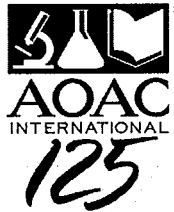
Appointees are Submitted for Review

Name, Affiliation, Contact Information

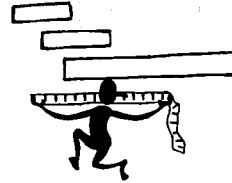
Are they: A Member AOAC? Can they submit a CV?

Have they filled out a VAF? Can they obtain a letter of support?

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Method Validation

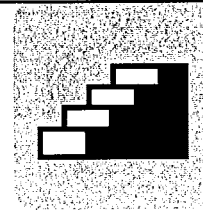


- **Simple definition: the systematic process of demonstrating the performance of a method of analysis.**
- **Answers the question: is the method fit for its intended purpose?**
- **Necessary for confident use of a method**

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Method Selection

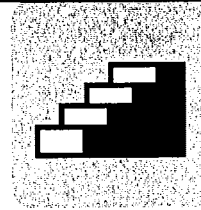


- **Identify Users/Needs/Problems**
- **Appoint Review Panel**
- **Literature Research**
- **Method Review & Assessment**
- **Assure Fitness For Purpose**
- **Evaluate Candidate Methods**
- **Selection or New Method Development**

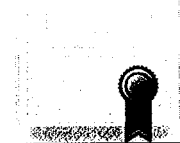
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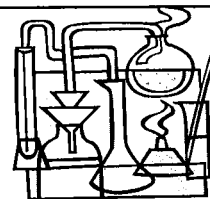
Method Validation



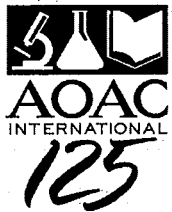
- **Method Optimization**
- **Single Laboratory Validation**
- **AOAC, OMB & Method Committee Review & Approval Of SLV & Proposed Study Protocol**
- **Complete Study & Address Comments/Issues**
- **Publish Manuscript in JAOAC**
- **Add To OMA**



Method Development



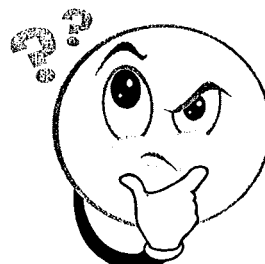
- The “fitness for purpose” of the method must be defined keeping in mind differing perspectives of all stakeholders
 - It should be reviewed and hopefully get by-in from potential users of the method and the data generated by the method
 - This “buy-in” will maximize its potential uses and applications
- Before submitting an application to AOAC to validate a method, it must be fully developed & optimized
 - Guidance is available through various AOAC resources
 - Follow the AOAC checklist and method format
- Having a well developed and optimized method will increase the chances of successful validation and utilization



Determining “Fitness For Purpose”

It Is Important To Assess Intended Applications Of Methods

- **What is the purpose of the method- how will stakeholders use it?**
 - Regulatory (will it be screening method or regulatory action method)
 - Product stability testing
 - Research & development
 - Process uniformity & quality assurance
- **Detection of what?**
 - Nutrients, adulterants, contaminants...
 - In what matrices
- **How often will the method be used?**
- **Who will use it? What labs? What analysts?**
- **What concentration ranges are expected?**
- **What (LOD's) & (LOQ's) are needed?**



Method Optimization

Develop and optimize all conditions

- Consider ways to optimize extraction/spectrophotometric/ chromatographic and other detection conditions
- Consider conditions for separation/quantitation of all analytes and from all expected matrices as well as other interferences
- Use reference materials and reference methods (if available)
- Ruggedness - testing the impacts of varying key parameters
- Understand strengths and weaknesses of critical steps

Use appropriate reference materials and separation techniques to identify and overcome interferences





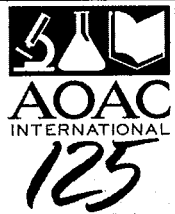
Be Sure You Measure The Analyte!



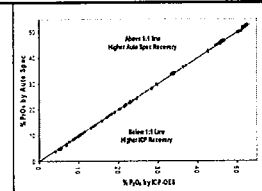
“Selectivity” and “Specificity”

- **Selectivity** – Is the ability to accurately measure the analyte in the presence of components that may be expected to be present in the sample matrix
- **Specificity** – The ability to assess unequivocally the analyte in the presence of components that may be expected to be present, such as impurities, degradation products, and matrix components.
- These can have different meanings in other disciplines (e.g. microbiology, DNA analysis)

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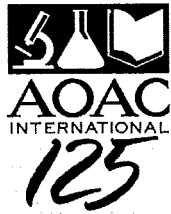


Calibration

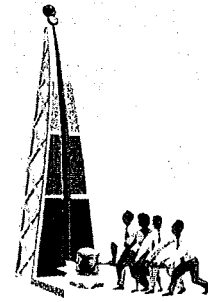


- Most calibrations use linear functions (i.e. Beer’s Law)
- Calibration functions must be validated over the entire intended range of the analyte measured by the method
- Specific calibrations should be generated for each analyte of interest
- Calibration requires the use of reference standards/materials
- Calibrations are most often thought of or expressed as linearity although they are not always linear
- Calibrations are sometimes instrument specific, they depend on vendor software to develop equations and perform calculations

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Why Do An SLV?



- To ensure viability of a method before doing a collaborative study
- To provide evidence of reliability in case a full collaborative study can not be completed
- To demonstrate that a method newly introduced into your laboratory is being properly performed
- As an internal laboratory proficiency check of current methods and practices

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What Is An SLV?

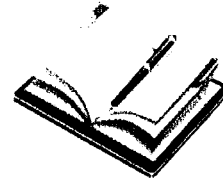


- Single-Laboratory Validation applies to a specific operator (or operators) and equipment in one laboratory/location
- It may account for:
 - Differences in equipment manufacturers or models
 - Differences in chemicals or laboratory standardized solutions
 - Differences in environmental conditions
 - Differences in personnel
- Additional SLV guidance and support is available through -
 - AOAC, ICH, USP/NF, EURACHEM, ISO/IEC, NMKL, FDA, US EPA
- It provides no information on inter-laboratory reproducibility!

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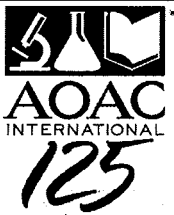


Prepare A Draft Method

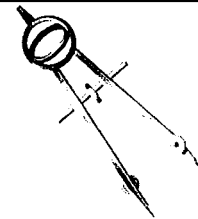


- It must be in AOAC style
- Using information gathered in the stakeholder meetings, literature research, method review and ruggedness testing it should be easy to –
 - Determine the scope and applicability of the proposed method
 - Predict method performance
 - Set goals for acceptability of the data generated
- How is this all possible? - I'll tell you

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Determine Scope & Applicability



- Samples for each matrix type specified in the scope and applicability must be obtained.
- Samples for each concentration range specified in the scope and applicability must be obtained or prepared
- Use real world samples when possible
 - They may introduce interferences & confounding conditions, but assure performance
- Samples should be -
 - Homogeneous (Non-uniformity in content/composition lead to poor validation results)
 - Prepared and stored in bulk by the managing laboratory
 - Checked to assure stability (protected from heat, light & moisture)
 - Designed to determine working concentration ranges and detection limits

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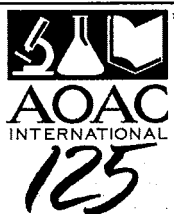


Determining Accuracy

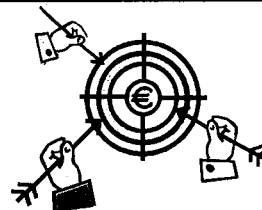


- **Method performance & accuracy can be determined by using**
 - Standard Reference Materials (SRMs)
 - Reference methods (if available)
 - Spike/recovery studies
- **Accuracy is inferred once linearity, precision, and specificity have been established**
- **Multiple preparations at several levels to determine mean & standard deviation at each level isolate random error versus bias**
- **Perform analysis on multiple days to help separate random error from the systematic error in the determination**
- **Accuracy can be determined in a single laboratory as it relates to that method in that laboratory**

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Determining Precision



- **ICH recommends performing a minimum of 9 determinations at 3 concentration levels (3 replicates at 3 levels) *or* 6 replicates at the 100% level**
- **Intermediate precision is to be established depending on “the circumstances under which the procedure is to be employed”**
- **Calculating expected precision is possible:**
 - **Expected RSD can be estimated from the Horwitz Equation:**

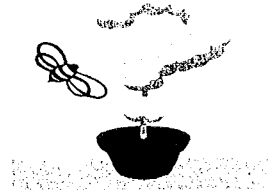
$$RSD_r = 2C^{-0.1505}$$

Where *C* is the concentration of analyte in the matrix, expressed as a decimal
As an example 100% = 1.0; 10% = 0.1; 1% = 0.01, etc.

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What Next?

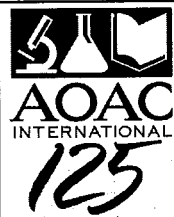


- **OMB has re-invented itself**
 - Learn how to use the new process & make it work for you
- **Work continues**
 - To harmonize the validation process & make it seamless
- **You can help by notifying the OMB & OMA editor of**
 - Potential errors, comments or harmonization issues

Contact Information -

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- OMA - Dr. George Latimer at latimerstx@verizon.net
- Presenter – Bill Hall at bill.hall@mosaicco.com

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Questions?

Thank You

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