

ISPAM Working Group on Qualitative Chemistry Method Guidelines
Hilton Rockville/Washington DC
Plaza I & II
June 30, 2011
10:45 am – 3:15pm

Presenters:

Jim Harnly, USDA-ARS BHNRC

Roy Macarthur, Food & Environmental
Research Agency, UK

Bert Pöpping ISPAM WG Chair, Eurofins

Paul Wehling, General Mills

Scott Coates, CSO AOAC INTERNATIONAL

Deborah McKenzie, Senior Director Methods
Approval Processes

1. Introductions:

Bert Pöpping, Eurofins and WG Chair provided an overview of the working group activities and discussed the objectives of the meeting. With that he introduced the day's presenters.

2. Presentations:

Jim Harnly, USDA-ARS BHNRC

Presented a power point on the "Draft AOAC Single Laboratory Validation of the Identification of [botanical or specific botanical material]". The presentation gave an overview of what distinguishes the SLV Botanical Identification Methods (BIM) from other methods of analysis. The (BIM) analyzes the whole material, not specific individual components, markers or analytes. Identification is based on comparisons of an unknown botanical material to the target material and utilizes inclusivity (non-target material) and exclusivity (target material) for measurement criteria and analytical measurement. The SLV method use a POD concept which was adapted to become a POI, Point of Identification and log-log calculation. Superior and inferior materials (acceptable/un-acceptable limits) need to be established and if there is a unknown non-target material, the BIM inclusivity panel determines mean spectra and variance.

Roy Macarthur, Food Environmental Research Agency, UK

“Draft Protocol for the Validation of Qualitative methods of Detection”, Joint IUPAC/MoniQA protocol for validation of qualitative methods.

Overview of why it is important to validate methods. The validation gives a prediction of the performance a method will possess when in use. Testing performed at “zero” and at least one other level is done to achieve target LOD and use of “positive” and “negative” results. The POD concept assists the validation method with the probability of “false” negatives and “false” positives. The Protocol takes into consideration inter-laboratory and single laboratory testing. Whereby the inter-laboratory tests at least 10 replicates under repeatability conditions and a prediction of the interval within which we can expect the probability of a false positive result to lie when the method is applied in a new laboratory. A prediction of the interval within expected false negative probability to lie at concentrations of interest. Hence, a prediction interval for limit of detection when the method is applied in a new laboratory. The Single Laboratory is all of the above, but on a new day.

Paul Wehling, General Mills

“Validation Scheme for Qualitative Analytical Method”, ISO Technical Committee 34, Standing Committee 16, Horizontal methods for molecular biomarker analysis, 2011 and “Probability of Detection (POD) as a Statistical Model for the Validation of Qualitative Methods.”

Discussion of the POD concept and its intimate correlation of assessing the parameters of probability of detection. Its versatility as part of any qualitative (binary) method. Probability will change with the concentration and as such the POD concept assists laboratories assess the suitability of a method of intended purpose by predicting the probability of a positive result in any given concentration. The POD concept is a simple statistic inherent in all other systems, such as Chi-Square, LOD, RLOD. The “POD Concept” is only new in that it recognizes the POD as a key parameter and plots a graph of POD vs concentration. The POD curve can be an indicator of the “usefulness” of the method. If POD were constant across all concentrations, the method would not be useful. Works for single lab and Multilab experiments. Works for paired and unpaired designs. Provides harmonization across qualitative/quantitative methodologies. Does comparisons and hypothesis tests via confidence interval analysis – equivalent to chi-squared tests. POD Curve plots mean response and uncertainty on the same graph.

Scott Coates, Chief Scientific Officer AOAC INTERNATIONAL

“Draft Standard Format and Guidance for AOAC Standard Method Performance Requirement (SMPR) Documents”

Coates reviewed the SMPR guideline that was developed in response to the number of SMPRs being written for a number of different projects. The guideline is a compilation of a number of existing AOAC guidelines and documents. The SMPR guideline covers chemistry and microbiology methods; and qualitative, quantitative, and identification

methods. The guideline provides guidance on the types of data required to validate methods. The guideline also include definitions of and recommendations for validation parameters such as reference method comparison, inclusivity/selectivity, exclusivity /specificity, environmental interference , laboratory variance, bias , and probability of detection (pod).

Scott Coates, Chief Scientific Officer AOAC INTERNATIONAL

“AOAC INTERNATIONAL Guidelines for Validation of Biological Threat Agent Methods and/or Procedures” (BTAM)

The Biological Threat Agent Methods and/or Procedures (BTAM) validation guideline was prepared in response to the development of a series of SMPRs for biological threat agents. The guideline was published in March 2011. The project to write the BTAM document was funded by the US Department of Defense and US Department of Homeland Security. The BTAM guideline was the first guideline to incorporate: 1) intended user testing; 2) test site definitions (as opposed to the traditional laboratory testing site); 3) instrument variation testing; and 4) the POD concept. The guideline is also the first document to allow for a reduction of collaborative study test sites.

Deborah McKenzie, Senior Director, AOAC Methods Development & Approval Processes

Hilde Skaar Norli, Nordic Committee on Food Analysis - Authored

“Guide in Validation of Alternative Proprietary Chemical Methods”, NordVal Protocol No. 2, Approved 26, May 2010

Deborah McKenzie presented on behalf of Hilde Skaar Norli to offer contrasts and similarities between NordVal protocol for validations and the previously reviewed presentations. NordVal resonates AOAC’s attitude of being a practical guide, a procedure that can be used by everyone, without requiring profound statistical knowledge. The NordVal protocol is based on a NMKL guide, NMKL Procedure No 20, 2007: "Evaluation of results from qualitative methods". The NMKL procedure has also an on-line excel spreadsheet to perform test calculations. Deviations from AOAC style validations include the use of kappa instead of POD concept to estimate agreement between the candidate and reference methods (or between the expected/true results and the obtained results). It also requires the use of 2 independent laboratories for confirmation instead of only 1 required by AOAC INTERNATIONAL. NordVal differs from previous protocols whereby it lends a definition of comprises a proprietary method.

Scott Coates, Chief Scientific Officer AOAC INTERNATIONAL

Comparison of Current Qualitative Chemistry Method Validation Guidance

Six guidelines were reviewed that specifically referenced recommendations for qualitative chemistry. The six documents are as follows:

MoniQA: Draft – “A Protocol for the Validation of Qualitative Methods of Detection” Roy Macarthur (Fera) & Christoph von Holst (IRMM), Joint IUPAC/MoniQA protocol for validation of qualitative methods, Monitoring & Quality Assurance (MoniQA) 2011

ISO: Draft- “ Validation Scheme for Qualitative Analytical Methods, ISO Technical Committee 34, Standing Committee 16

SMPR: Draft- “Standard Format & Guidance for AOAC Standard Method Performance Requirement (SMPR) Documents”, version 12.1; 31-Jan-11

Bot ID: Draft- “Single Laboratory validation of the identification of [botanical or specific botanical material] AOAC Expert Review Panel for the Validation of Identity Methods for Botanical Raw Materials, AOAC INTERNATIONAL, 2011

NordVal: “Guide in Validation of Alternative Proprietary Chemical methods, NordVal Validation, NordVal Protocol No. 2, Approved 26, May 2010

BTAM: “AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Biological Threat Agent Methods and/or Procedures (BTAM), Journal of AOAC INTERNATIONAL VOL. 94, NO. 4, 2011

The guidelines contain many similar concepts with differences specific to the application. The POD concept is prevalent throughout the guidelines.

Bert Pöpping, ISPAM WG Chair, Eurofins

Definition of Qualitative Chemistry Methods

Qualitative methods test for either “positive” or “negative”, not corresponding concentration. Any method that gives a binomial response can be considered a qualitative method. A good example of qualitative method would be real-time PCR. The PCR results can be both, qualitative and quantitative with its binary evaluation. It was proposed during the Working Group meeting that perhaps the PCR results be taken in to groups. One using the binary results, and the second group use the results in a further detailed analysis. This discussion will be continued at future meetings.

All of the presentations listed above are available on line at the ISPAM page. While on our website, please take a moment to review the up-coming AOAC INTERNATIONAL Annual Meeting agenda, being hosted in New Orleans, Louisiana, USA on September 18-21st, 2011.