

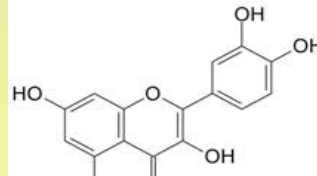
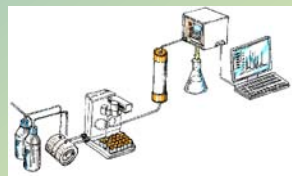


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Comparison of Qualitative Chemistry Validation Guidelines

Gaithersburg, Maryland, USA

Thursday June 30, 2011





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Guidelines Compared

- 10 documents were posted on the ISPAM website for information.
- Only guidelines with recommendations for specifically for qualitative methods were selected for comparison.
- 6 guidelines were selected for comparison.



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- 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 and Quality Assurance (MoniQA), 2011.
- ISO Draft *Validation Scheme for Qualitative Analytical Methods*, ISO Technical Committee 34, Standing Committee 16
- SMPR Draft *Standard Format and Guidance for AOAC Standard Method Performance Requirement (SMPR) Documents* (Version 12.1; 31-Jan-11)



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- 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



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Organization of Comparisons

- Parameter
 - Each guideline term for parameter
 - Definition
 - Recommendations
- Notes
- Summary



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Inclusivity - Selectivity



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SMPR

inclusivity & selectivity

Strains or isolates or variants of the target agent(s) that the method can detect.

Analyze one test portion containing a specified concentration of one inclusivity panel member. **Panel developed by MC.**

BTAM

inclusivity

The strains or isolates or variants of the target agent(s) that the method can detect.

Analyze one test portion containing **at AMDL** of one inclusivity panel member. **Panel developed by MC.**

NordVal

inclusivity

the ability to detect the relevant members of a target analyte group or the target analyte from a wide range of sources

Analyse samples from **different regions/countries** to determine if the method can detect the analyte.

Bot ID

inclusivity

Ability to correctly identify variants of the target material that meet **the identity specification.**

Test samples from an inclusivity/exclusivity panel. Does not specify number of samples or replicates.



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Notes

- ISO and MoniQA did not contain information on inclusivity



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Inclusivity Summary

BTAM

- specifies AMDL
- Inclusivity panels designated by MC.

NordVal

- regional variants
- Bot ID
 - Identity speciation in place of inclusivity panel.



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Exclusivity - Specificity



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SMPR

Exclusivity/Specificity

Strains or isolates or variants of the target agent(s) that the method must not detect.

Analyze one test portion containing a specified concentration of one exclusivity panel member. **Panel developed by MC.**

BTAM

Exclusivity

The nontarget agents, which are potentially cross-reactive, that are not detected by the method.

Test one replicate per strain/substance at **10X AMDL** using the method. **Panel developed by MC.**

NordVal

Specificity, SP

Ability to distinguish the analyte from other substances present in the sample. SP = proportion of test samples that do not contain the analyte and respond negatively to the test.

Bot ID

Exclusivity

Ability of a method to correctly reject non-target botanical materials.

Test samples from an inclusivity/exclusivity panel. Does not specify number of samples or replicates.



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Notes

- ISO and MoniQA do not contain information on exclusivity



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Exclusivity Summary

BTAM

- Exclusivity panels designated by MC.
- Specifies testing 10X AMDL

SMPR

- Similar to BTAM without AMDL

NordVal

- Uses the term “specificity”; does not prescribe testing.



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Notes

- ISO and MoniQA do not contain information on exclusivity



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Analytical Response



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BTAM

POD

Proportion of positive analytical outcomes for a qualitative method for a given matrix at a given analyte concentration.

No recommendations. Number of levels and replicates to be determined by an ERP.

SMPR

POD

Same as SMPR

Same as SMPR.

NordVal

Sensitivity (SE)

Sensitivity = proportion of positive results with truly positive samples.

The relative sensitivity (SE) is the ability of a method to detect the analyte compared to a reference method.

No recommendations regarding the number of levels and replicates.



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Bot ID

Analytical Response Curve

– POI

Probability of Identification (POI)
= The expected or observed fraction of test portions at a given concentration that give a positive result.

Test samples with various conc. of target, determine POI. No recommendations regarding the number of levels and replicates.

MoniQA

POD

Refers to the POD model and cites Wehling

. . . n blind-replicate samples that do not contain the analyte, and m blind-replicate samples*

ISO TC34 SC16

Refers to the POD model and cites Wehling



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Note on MoniQA

- that contain the analyte at a concentration no higher than the target limit of detection sent to each of L laboratories such that nL negative results confirm that the false negative probability is sufficiently low and mL positive results confirm that the false negative probability at the limit of detection is sufficiently low.



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Notes

- Bot ID guideline introduces Probability of Identification (POI). Similar in concept to POD.
- 5 of 6 guidelines refer to POD or POI.



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Reference Method Comparison



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SMPR

Reference method comparison

Mentioned but no definition

No recommendations.

NordVal

Agreement between methods/replicates, κ (kappa)

Measures agreement between methods.

κ calculated using the accuracy and the frequency of agreement or repeatability by chance.

$\kappa \leq 0.20 \rightarrow$ Poor agreement

$\kappa \in \{0.21 - 0.40\} \rightarrow$ Fair agreement

$\kappa \in \{0.41 - 0.60\} \rightarrow$ Moderate

$\kappa \in \{0.61 - 0.80\} \rightarrow$ Good agreement

$\kappa > 0.80 \rightarrow$ Very good agreement



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Notes

BTAM, ISO TC34 SC9, MoniQA, and Bot ID do not mention reference method comparisons.



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Collaborative Studies



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BTAM

Collaborative study

A minimum of 12 collaborators.

At least 10 valid data sets.

The study must include a minimum of three test sites with no more than four collaborators at any one test site.

Calculate
POD(0), POD(C), CPOD

SMPR

Collaborative study

No minimum recommendations.

Calculate
POD(0), POD(C), CPOD

NordVal

Intermediate study

A study of the proprietary method's performance by at least one additional independent laboratory.

At least 3 food materials, spiked at 3 levels (low, medium and high) and a negative control.

The lowest level should be about the detection/screening level. If the intermediate study is conducted at only one additional laboratory the number of replicates for each matrix has to be at least five.



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ISO

TC34 SC 16

Collaborative study

≥ 10 laboratories

12 replicates/laboratory

Calculate POD.

MoniQA

Collaborative study

Refers to the POD model
and cites Wehling

. . . n blind-replicate samples
that do not contain the
analyte, and m blind-
replicate samples. *

*See previous note.

Bot ID

Collaborative study

≥ 10 laboratories

12 replicates/laboratory

Calculate and report the
POI results with
confidence intervals for
each laboratory, and for
the combined results.

Estimate reproducibility.



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Unique Parameters - NordVal

Relative accuracy

the degree of correspondence between the response obtained by the proprietary method and the reference method on artificially contaminated samples, or “the expected/true” results of the spiked samples.



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Unique Parameters - NordVal

Detection Capability (CCb)

the smallest content of the substance that may be detected, identified and/or quantified in a sample with an error probability of β . The β error is the probability that the tested sample is truly non-compliant even though a compliant measurement has been obtained. For screening tests the β error (i.e. false compliant rate) should be $< 5\%$.



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Unique Parameters – Bot ID

**Specified superior test material (SSTM) and
Specified inferior test material (SITM)**

SSTM - a botanical material mixture that has the minimum acceptable concentration of the target material, as specified by an SMPR.

SITM - a botanical material mixture that has the maximum concentration of target material that is considered unacceptable, as specified by an SMPR.



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Unique Parameters - BTAM

Test sites

Sites that simulate where the method is intended to be used.

Environmental Interference

Determine the POD at the AMDL and P(0) with potential inhibitors and cross-reactive cmpds.



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Unique Parameters - SMPR

Environmental Interference

Determine the POD at the AMDL and $P(0)$ with potential inhibitors and cross-reactive cmpds.



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Unique Parameters - MoniQA

Prediction interval for the POD

Results are used estimate a prediction interval for the probability of detection when the method is applied in a new laboratory at each concentration.

- Prediction intervals are plotted to estimate upper and lower limits for the limit of detection and false positive probability.



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Summary

- Guidelines contain many similar concepts.
- Differences are usually specific to the application.
- POD model prevalent.