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AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Biological Threat Agent Methods and/or Procedures

(BTAM)

Gaithersburg, Maryland, USA

Thursday June 30, 2011





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Background

- AOAC microbiology guidelines did not apply very well to biological threat agents.
- Needed a new set of guidelines and a new Methods Committee (L).
- Major questions about the number of labs available for collaborative study.



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Background

- Started process of writing BTAM guideline in 2008.
- Sponsored by DOD in 2008; sponsored by DHS 2009 and 2010.
- Reviewed by Committee L.
- Published in 2011.



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New Concepts Introduced

- Probability of Detection (POD)
- Acceptable Minimum Detection Level (AMDL)
- Between Instrument Variation Study
- Intended Use Matrix Study/ Test Sites



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Probability of Detection (POD)

- Proportion of positive analytical outcomes for a qualitative method for a given matrix at a given analyte concentration
- POD is concentration dependent



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Acceptable Minimum Detection Level (AMDL)

- A predetermined minimum level of a biological threat agent specified by the Methods Committee . . . , which must be detected by the candidate method with . . .
.. POD of 0.95 or higher.



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Between Instrument Variation Study

- A study designed to ensure that the performance of the method is consistent from instrument to instrument.



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Intended Use Matrix Study

- The purpose of the intended use matrix study is to measure the POD at the AMDL or lower under simulated intended use conditions with representative end users for all matrixes claimed in the intended use statement.



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Test Sites

- Sites that simulate where the method is intended to be used, such as:
 - Traditional laboratory.
 - Mobile laboratory.
 - Non-laboratory indoor facility.
 - Outdoor mobile site.
 - Outdoor automated stationary site.



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Test Parameters

- Inclusivity
- Exclusivity
- Intended Use/Lab Matrix Study
- Environmental Interference
- Robustness, Product Consistency & Stability



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Test Parameters

- Instrument Variation
- Collaborative Study



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Inclusivity

- Test one replicate per strain/substance at the AMDL.
- If an individual inclusivity panel member tests incorrectly, retest with 96 replicates, with no failures allowed = POD of 0.95 or higher.



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Exclusivity

- Test one replicate per strain/substance at the 10X AMDL.
- If an individual exclusivity panel member tests incorrectly, retest with 96 replicates, with no failures allowed = POD of 0.95 or lower.



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Intended Use/Lab Matrix Study

- 96 inoculated test portions at AMDL or lower concentration for each matrix. 96 test portions of matrix inoculated with near neighbor at 10X AMDL as negative controls.
- Types of environmental matrixes described: nonporous surfaces, air collection filters, air collection into aqueous solution, soils and bulk powders.



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Intended Use/Lab Matrix Study

- Report each matrix individually.
- Estimate the POD with a 95% confidence interval for the candidate method and, if included, the presumptive and confirmed results.



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Environmental Interference

- Exact environmental contaminants to be determined by Committee L.
- Evaluate for cross-reactivity and inhibition.



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Robustness, Product Consistency & Stability

- Standard AOAC guidance similar to the microbiology method guideline.



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Instrument Variation

- Minimum of six instruments.
- For continuous numerical output:
 - test 5 replicates of each agent and near neighbor concentration for each instrument.
- For binary sensors:
 - test 96 replicates per instrument of agent at the AMDL and 96 replicates per instrument of a near neighbor at 10X AMDL.



Collaborative Study

- The collaborative study must include a minimum of 12 collaborators.
- After eliminating data sets for assignable cause, the study must yield 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.



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Quantitative Section

- Not of interest for today's discussion, but the guideline does address validation of quantitative methods.
- Guideline does not address validation of identity methods.



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Summary

- Quite prescriptive.
- Quite detailed.
- Several new concepts.
- Describes what must be done. SMPRs describe minimum acceptable results.