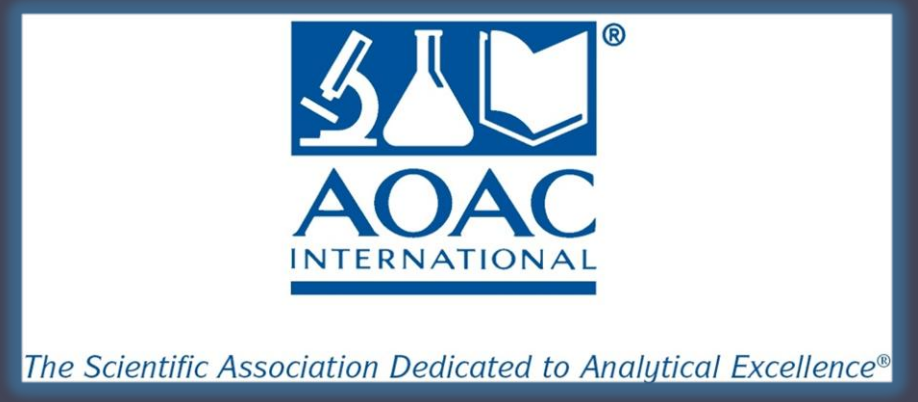

Expert Review Panel for SPSFAM Select Food Allergen Methods

(SPSFAM)

MONDAY, MARCH 13, 2017, 8:00 a.m.
Room: Salon C-D-E

MARRIOTT WASHINGTONIAN CENTER
9751 WASHINGTONIAN BLVD,
GAITHERSBURG, MARYLAND
UNITED STATES

contact: spsfam@aoac.org

Expert Review Panel for SPSFAM Select Food Allergen Methods

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contact: spsfam@aoac.org

SPSFAM Food Allergens ERP Chair:
Dr. John Szpylka, Mérieux Nutrisciences

Dr. John Szpylka is the Scientific Affairs Director, Chemistry N.A. with Mérieux NutriSciences where he manages nutritional analytical method development for Mérieux NutriSciences and is a technical leader for chemistry testing in North America. John is a representative to key scientific organizations and regulatory agencies to identify and contribute to food testing standardization for nutritional needs and arising issues. This includes active involvement in organizations including AOACI, AACCI, AOCS, AAFCO, ACIL, and DSQAP. John Szpylka is a Fellow of AOAC International and is a past chair of the *AOAC Official Methods Board*. He currently serves on numerous Stakeholder Panels and Expert Review Panels. John also serves as a Board Member for the American Council of Independent Laboratories. Before joining Mérieux NutriSciences, John was a Principal Scientist with General Mills / Medallion Laboratories where he oversaw the development and operation of food analytical methods.

John received his doctorate in analytical chemistry from the Ohio State University after receiving a B.S. in chemistry from Rensselaer Polytechnic Institute.

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SPSFAM EXPERT REVIEW PANEL (ERP) FOR SELECTED FOOD ALLERGENS

Full Name	Position	Organization
John Szpylka	Chair	Mérieux NutriSciences
David James Almy	Member	Neogen Corporation
Sneh D. Bhandari	Member	Merieux NutriSciences
France Cho	Member	Maxxam Analytics
Dr. Ken Davenport	Member	3M
Melanie Downs	Member	University of Nebraska-Lincoln
Stefan Ehling	Member	Abbott Nutrition
Michael John Farrow	Member	Abbott Nutrition
John Lawry	Member	Covance
Linda Monaci	Member	CNR Italy
Minh Hai Nguyen, Sr.	Member	Thanglong Instruments
Yasutaka Nishiyama	Member	NH Foods Ltd.
Bert Popping	Member	Consultant
Susanne Siebeneicher	Member	R-Biopharm AG
Tomasz Tuzimski	Member	Medical University Of Lublin
Sudhakar Yadlapalli	Member	First Source Laboratory Solutions LLP
Wei Zhu	Member	Danone
Jerry Zweigenbaum	Member	Agilent Technologies, Inc.
Scott G. Coates	AOAC Staff	AOAC INTERNATIONAL
Christopher Dent	AOAC Staff	AOAC INTERNATIONAL
Dawn L. Frazier	AOAC Staff	AOAC INTERNATIONAL

The Scientific Association Dedicated to Analytical Excellence®

AOAC Stakeholder Panel on Strategic Food Analytical Methods

Expert Review Panel for Selected Food Allergens

Monday, March 13, 2017, 8:00 a.m. – 12:00 a.m.

Marriott Washingtonian Center, Salon C-D-E

A G E N D A

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1. Welcome and Introductions
   John Szpylka, Mérieux NutriSciences (ERP Chair)

2. Review of AOAC Volunteer Policies & ERP Process Overview and Guidelines
   Deborah McKenzie, AOAC INTERNATIONAL

3. Method Developer Presentation
   Hua-Fen Liu, SCIEX

4. Review of Methods
   For each method, the assigned ERP members will present a review of the revised method manuscripts, after which the ERP will discuss the method and render a decision on the status for each method.

   A. ALL-01
      a. Linda Monaci Review
      b. Sneh Bhandari Review
      c. Other Submitted Reviews
      d. Discussion and Vote

5. Final Action Requirements for Approved Method(s)

6. Adjourn

AOAC Expert Review Panels

2016 ERP Orientation and Logistics

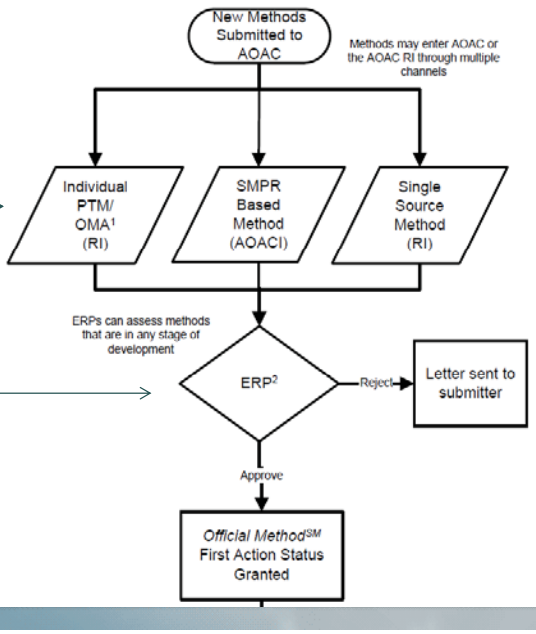
Road to First Action OMA Status

Terms:

- PTM – *Performance Tested Methods℠*
- RI – Research Institute
- ERP – Expert Review Panel
- OMB – Official Methods Board
- SP – Stakeholder Panel
- SMPR – Standard Method Performance Requirement

Three modes of entry and (program administration)

Expert Review Panels will review all methods for all three modes of entry.

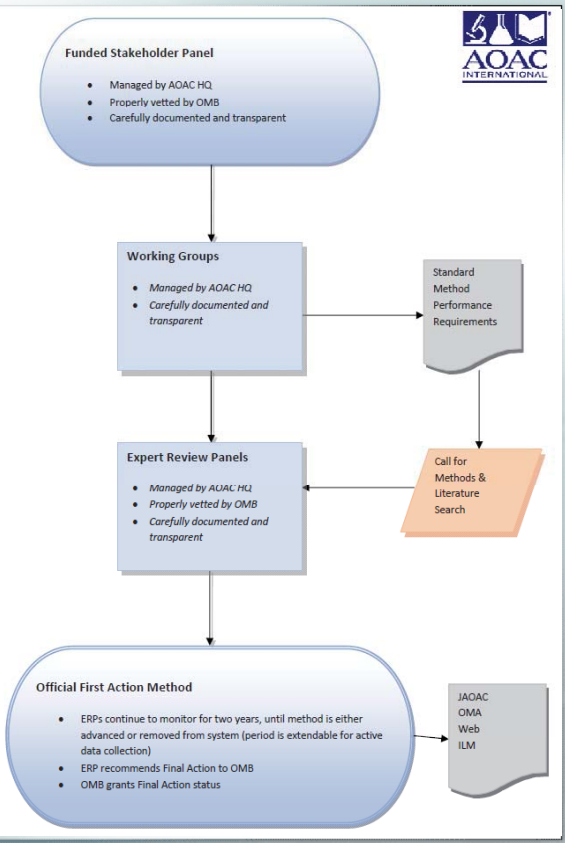


Note: Appeals process always available; see Alternative Pathway Guidelines for appeals process.

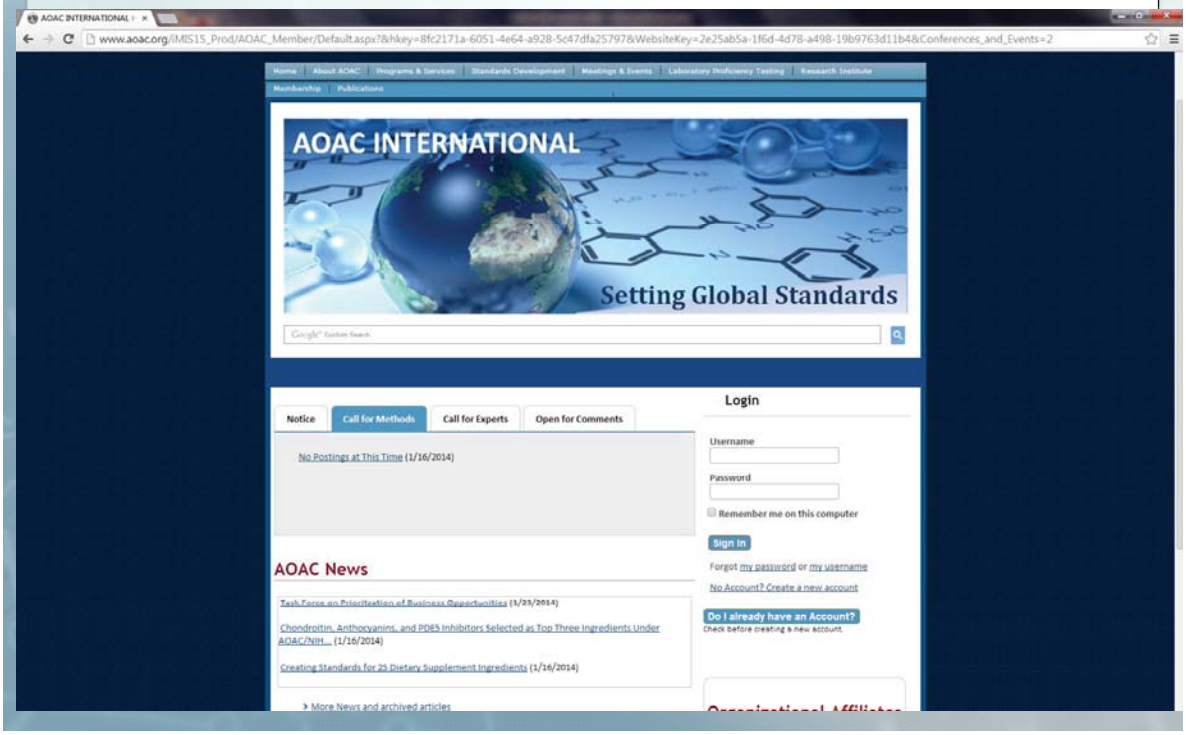
1 PTM certification previously issued, PTM reviewers will be ERP members
2 Unless otherwise provided for under a contractual agreement, AOAC will regularly convene ERPs twice a year: once during the Mid-Year Meeting and again during the Annual Meeting

Recap of the Overall Process for Methods Submitted in response to SMPRs or Call for Methods – aka "alternative pathway"

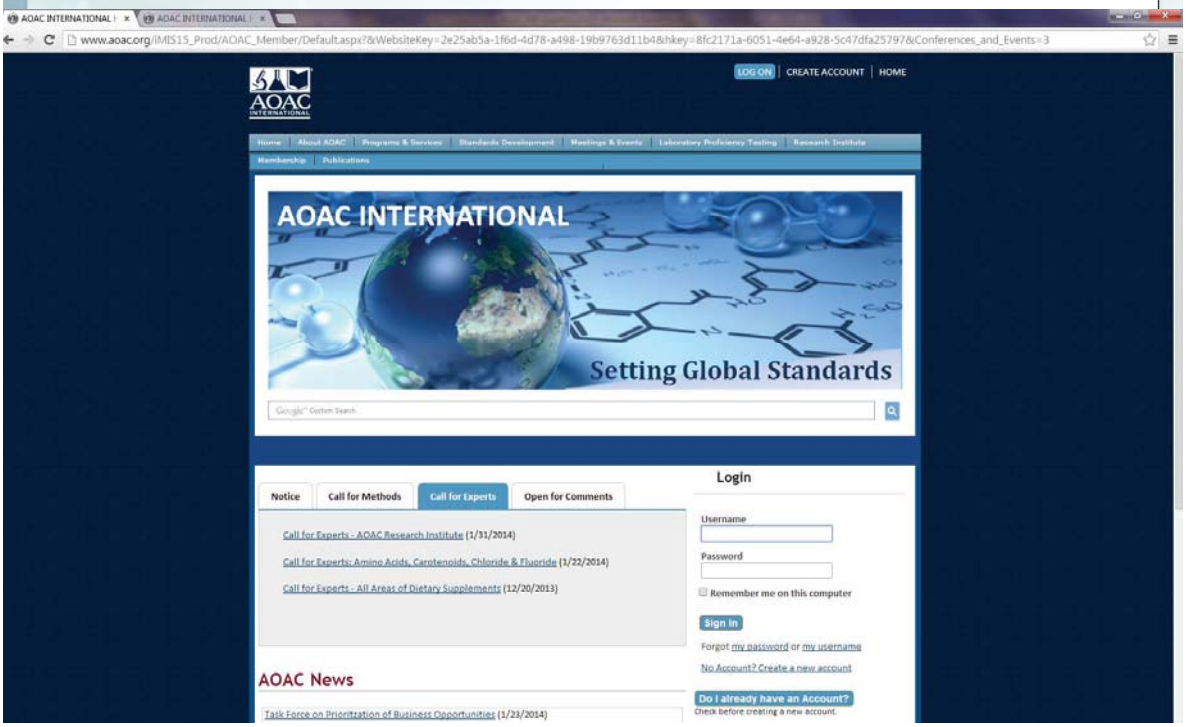
1. Allows AOAC to focus on projects addressing an urgent need of a critical mass of stakeholders.
2. Drives AOAC processes forward faster.
3. Assembles stakeholders (industry, government and academia) to neutral place to articulate and reach consensus on requirements and resolve conflicts.
4. Those requirements are codified and are published as "Standard Method Performance Requirements" (SMPRs).
5. Methods are solicited that purport to meet those requirements.
6. Expert review panels (ERPs) judge the methods against the SMPRs. Method(s) that best meet the SMPRs are adopted and designated "First Action" *Official Method of Analysis*.
7. Process for First Action status to Final Action status follows as the same process for all AOAC First Action *Official Methods*.



Calls for Methods



CALL FOR EXPERTS



Other Forms of Recruitment

- Official Methods Board
- Email Blasts to AOAC network
- Leveraging networks of Advisory Panel members, Working Group Members, AOAC Communities and Sections

REQUIREMENTS FOR ERP SERVICE

- Must have demonstrated expertise in the method, technology, analyte/matrix, etc… Be a subject matter expert.
- Must be able to attend ERP meetings
- Must be able to complete assigned reviews on time
- Must be prepared to speak on the method and share reviews during the meeting
- Must be proactive in tracking assigned First Action *Official Methods*
- Must be able to assist in peer reviewing paper for publication
- Must sign and submit AOAC Volunteer Acceptance Form

AOAC Policies

- AOAC INTERNATIONAL Antitrust Policy
- AOAC INTERNATIONAL Policy On The Use Of The Association Name, Initials, Identifying Insignia, Letterhead, And Business Cards
- AOAC INTERNATIONAL Policy And Procedures On Volunteer Conflict Of Interest
- Volunteer Acceptance Form

Vetting Process

AOAC Chief Science Officer

- Reviews all candidates and supporting documentation for expertise
- Makes a recommendation for an ERP slate

Official Methods Board

- Reviews proposed recommended ERP slate
  - Expertise
  - Balance of panel
  - Conflicts of interest
- Renders decision on proposed ERP members and a Roster is formed.

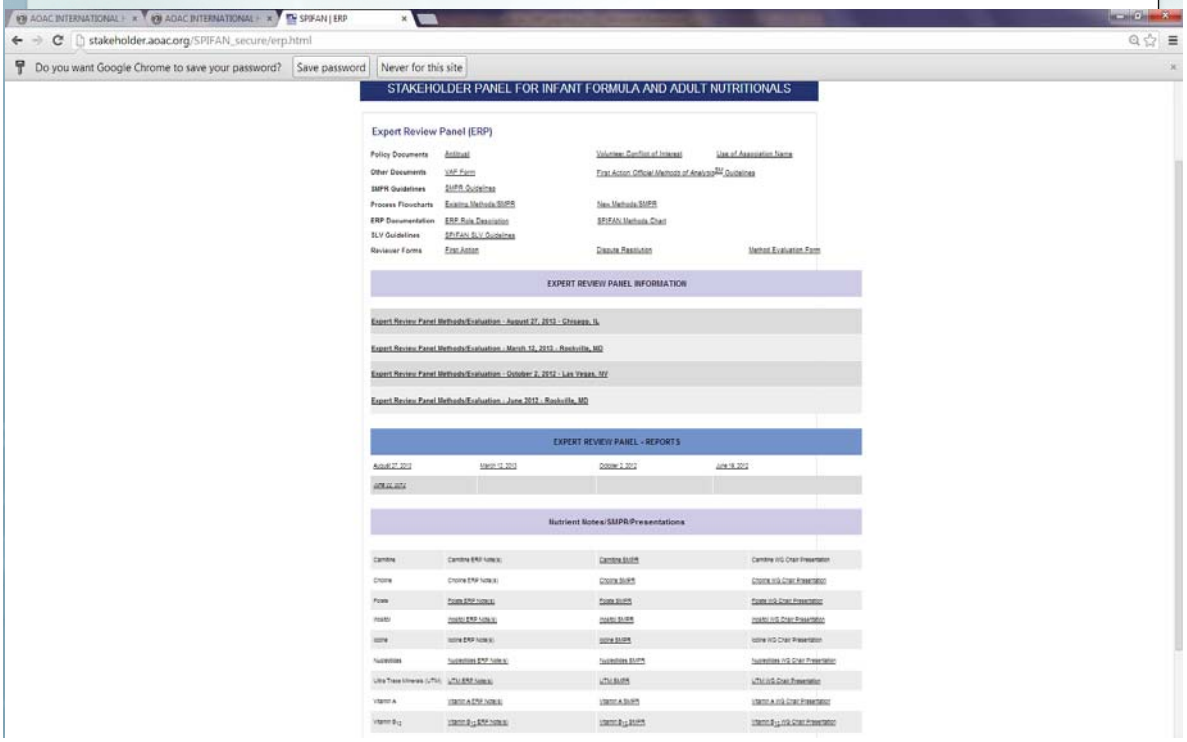
ERP Method Assignments

- A primary and secondary reviewer is assigned to every method.
  - In depth review via review form
  - Prepare to attend and speak on the method and make a recommendation for ERP discussion and consideration.
  - Review forms are completed and returned to AOAC staff in advance of the meeting.
- For Research Institute method submissions:
  - ERP members can participate in the Consulting Service conducting review of protocols – electronically.
- Members of both Committee on Safety and Committee on Statistics serve as advisory resources for all ERPs

ERP REVIEWS

- Primary and Secondary Reviewers or entire ERP (Research Institute ERPs) conduct in-depth review of method and any supporting information.
  - In-depth review is done electronically through password protected website access and is completed prior to the in-person meeting.
  - Deadlines for submission of reviews
  - Depending on the number of methods 15 to 30 days for review
  - Track and present feedback on assigned First Action *Official Methods*.
  - Present on the method during the meeting and can make the motion to adopt the method.
  - Can recommend additional feedback or information for Final Action consideration

ERP REVIEWS



ERP REVIEWS

- **In your judgment, does the method sufficiently meet the Standard Method Performance Requirements (SMPR) or community-based guidance?**

- In your judgment, is the method scientifically sound and can be followed?
- In your judgment, what are the strengths and weaknesses of the method?
- In your judgment, how do the weaknesses weigh in your recommendation for the method?
- In your judgment, will the method serve well the stakeholder community that will use the method?
- In your judgment, what additional information may be needed to further support the method meeting the SMPR or community-based guidance?

ERP Meetings

- ERPs will meet in person at a minimum of twice a year and up to four times per year:
  - AOAC Mid-Year meeting (DC metro area)
  - AOAC Annual Meeting.
  - 2 additional designated times for proprietary method Organziational Affiliates
- At the ERP meeting:
  - Primary and secondary reviewers or entire ERP will present their reviews and makes a motion/recommendation to the ERP whether or not to adopt the method as First Action OMA.
  - ERP discusses the method.
  - ERP renders a decision on First Action status.
  - ERP renders decisions on modifications to First Action methods only.
- If the method is adopted
  - ERP decides on what additional information is needed to recommend the method for Final Action status

ERP MEETINGS

- MEETINGS ARE HELD IN-PERSON, HOSTED BY AOAC
- A QUORUM IS THE PRESENCE OF SEVEN (7) MEMBERS OR 2/3 OF THE TOTAL VETTED ERP, WHICHEVER IS GREATER.

IF NO QUORUM, THEN NO MEETING!

ERP MEETINGS

- REVIEWERS PRESENT THEIR REVIEWS AND MAY INITIATE A MOTION TO ADOPT THE METHOD IF THEY CHOOSE
  - Chair recognizes the reviewers
  - Primary and secondary / ERP reviews are presented.
    - If in favor, they may make and second a motion to adopt or not adopt the method
    - Chair can then entertain discussion on the method
    - Chair can call for a vote once deliberation is complete

ERP MEETING - Discussions

- In your collective judgment, is the method scientifically sound and can be followed as written?
- **In your collective judgment, does the method sufficiently meet the Standard Method Performance Requirements (SMPR)?**
- In your collective judgment, what are the strengths and weaknesses of the method?
- In your collective judgment, do the weaknesses outweigh the strengths in your recommendation for the method?
- In your collective judgment, is the method safe and can it serve well the stakeholder community that will use the it?
- In your collective judgment, is additional information needed to before considering this method for First Action OMA status?

ERP CONSENSUS

- First Action Official Methods status is granted:
- Method must be adopted by unanimous decision of ERP on first ballot, if not unanimous, negative votes must delineate scientific reasons.
- Negative voter(s) can be overridden by 2/3 of voting ERP members after due consideration.
- Method becomes First Action on the date when ERP decision is made.

ERP CONSENSUS

- The ERP may then reach consensus on any additional information that it needs to review to be able to make a recommendation for Final Action *Official Methods* status.
- This is a separate motion.

Post ERP Meeting

- An ERP report with the decisions of the ERP will be drafted
  - Review and approval by ERP chair
  - Posted on website within 15 business days after the ERP meeting
- AOAC staff will send notification to method authors/submitters regarding outcomes on specific methods

ERP Tracking

- Between First Action and Final Action:
  - The primary and secondary reviewers track the methods on behalf of the ERP over this time period.
    - Based on information from method authors, laboratories using the method, general community feedback, additional laboratory work
    - Are ERP recommendations being fulfilled?
    - Is the method meeting the standard criteria more closely?
    - How well is community guidance and OMB guidance being reflected?
  - Updates on the method are given by the primary and secondary reviewers during the ERP meetings.
  - At the end of two years, ERP makes a recommendation to OMB for Final Action status, repeal, or continuance.

Road to Final Action OMA Status

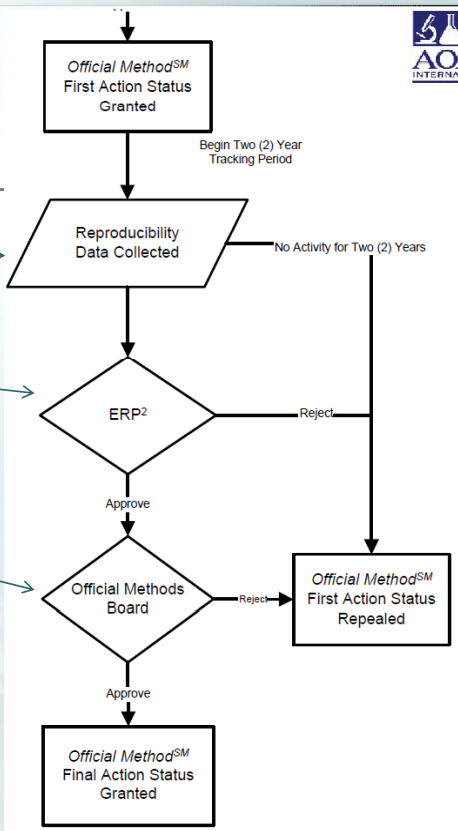
Method reproducibility must be demonstrated before Final Action consideration.

ERP determines if sufficient evidence merits a recommendation for Final Action status or repeal.

•Only the OMB promotes a method to "Final Action" status or repeal the method.

•Methods that did not meet the bar would be repealed.

•Same for all method submissions



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Path to Final Action

Review of ERP Method Recommendations

What to Expect from AOAC Official Method Board (OMB)

Standard Method Performance Pathway

1. Standard Method Performance Requirements authored by Working Groups and established by Stakeholders
2. Expert Review Panel (ERP) vetted by OMB
3. ERP approves methods for First Action
4. Method reproducibility data collected
5. ERP monitors method performance
6. ERP recommendations sent to OMB within 2 years
   - Final Action, First Action continuation, or Repeal

OMB Liaison

- OMB member or designee is assigned to your ERP
- Liaison monitors First Action to Final Action process
- Monitors ERP's documentation of all items in OMB Guidance document (OMA Appendix G)

Method Applicability

- Determine how method meets stakeholder's needs
  - scope, accuracy, precision, etc.
- Are ERP recommendations & improvements implemented?
- Assess method limitations & concerns

Safety Concerns

- Safety review completed for First Action
  - Participation by Safety Committee
- All safety issues identified during 2 year review addressed
  - Participation by Safety Committee

Reference Materials

- Identification of potential reference materials (RM)
  - If none found, define alternative options
- RM performance expectations

Available resource is the AOAC Technical Division on Reference Materials (TDRM)

Single Laboratory Validation

Chemistry

- Linearity
- Accuracy
- Repeatability
- LOD / LOQ
- Matrix scope
- Selectivity

Microbiology

- Inclusivity/Exclusivity
- Robustness
- Repeatability
- POD or equivalent
- Matrix scope

AOAC Committee on Statistics is your resource

Quantitative Reproducibility/Uncertainty

- Experimental designs may vary
  - Collaborative study
  - Proficiency Testing data
  - Multi-lab study variations
- Committee on Statistics
  - is available to discuss new study design protocols
  - Formalized tools were presented at the 2013 Annual Meeting

Qualitative Reproducibility/Uncertainty

- Experimental designs may vary
- Committee on Statistics is available to discuss new study protocols designs

Compare to SMPR

- Method meets Performance Criteria
- Method does not meet Performance Criteria
  - Acceptable or not? List reasoning
- Document acceptability to Stakeholders

Feedback from Users

- Solicit and document user feedback
  - ERP Chair determines mechanism
  - May take form of
    - Proactive calls to users
    - Tally of incoming calls
    - Emails
    - Web surveys

Feedback from Users

- Method performance
- Safety Concerns
  - Warnings
  - Alternatives
- Equipment and supply availability
  - Readily available
  - Practicality
  - Suggested improvements
  - Failures
- Reference material availability

ERP Recommendations

- Supply all documentation to AOAC by established deadline
  - Documentation includes ERP review details
- Representative from ERP present at OMB review meeting
- If method to be repealed, document reasoning

Publication of First Action Methods

- Any approved method(s) along with supporting manuscript(s) and documentation sent to AOAC Publications after the meeting.
  - AOAC Official Methods number assigned.
  - Method and method manuscript prepared for publication in the *Official Methods of Analysis of AOAC INTERNATIONAL* and in Journal of AOAC INTERNATIONAL
  - Updates on methods approved or status changes are published in the Inside Laboratory Management magazine and on the AOAC website

Publication of First Action Methods

NO OMA NUMBER ASSIGNED

UNTIL ALL DOCUMENTATION SUBMITTED

1. Method incorporating ERP revisions (preferably in AOAC Format)
2. Method Manuscript incorporating ERP revisions (in AOAC Format)
3. Signed AOAC Copyright Authorization form

Reports and Documentation

- AOAC staff or designee will capture the decisions and action items into an ERP report.
- The draft report will be sent back to the ERP Chair whose responsibility it is to sign off on the report once approved.
- The report is then distributed to the ERP.
- ERP is responsible for a drafting a written recommendation to the OMB for each method at a maximum of two years following adoption as First Action OMA
- Approved methods from the ERP meetings are published in the OMA and in the *Journal of AOAC INTERNATIONAL*.
- Meeting overviews are published in the AOAC *Inside Laboratory Management* magazine.

Roles and Responsibilities

- Expert Review Panel:
  - Review methods and meet in person to discuss and render decisions on methods for First Action *Official Methods* status.
  - Track First Action *Official Methods*
  - Modify First Action methods if necessary
  - Make recommendations on First Action methods no more than 2 years after adoption to OMB.
- Official Methods Board:
  - Vet and approve ERP membership
  - Assign OMB liaison to be a resource to the ERP
  - Review ERP recommendations and render decisions (*Final Action, Repeal or remain First Action*) on First Action OMAs
- AOAC Staff
  - Coordinate the ERP and meetings, facilitate reviews, document ERP actions/decisions.
  - Issue necessary calls for experts and methods

Expert Review Panels

The ERPs review and approve appropriate methods (as submitted or modified) for adoption as First Action Official Methods or for further validation. ERPs also make recommendations regarding Final Action Official Methods status.

Expert Review Panels

- Must be supported by relevant stakeholders.
- Constituted for the review of methods, not for Standard Method Performance Requirements (SMPR) purposes or as an extension of a Working Group.
- Consist of a minimum of seven (7) members representing a balance of expert stakeholders. **Quorum is a minimum of 7 members present or 2/3 of the total vetted members, whichever is greater.**
- ERP constituency must be approved by the Official Methods Board (OMB).
- Holds transparent public meetings only.
- Remains in force as long as method in First Action Status.

First Action Official Method Status decision

- Must be made by an ERP constituted or reinstated post 2011-03-28 for First Action Official Method Approval (FAOMA).
- Must be made by an ERP vetted for FAOMA purposes by OMB post 2011-03-28.
- Method adopted by ERP must perform adequately against the SMPR set forth by the stakeholders. Or demonstrate performance or characteristics that meet the scope, applicability and/or claims of the method.
- Method must be adopted by unanimous decision of ERP on first ballot, If not unanimous, negative votes must delineate scientific reasons.
- Negative voter(s) can be overridden by 2/3 of non-negative voting ERP members after due consideration
- Method becomes First Action Official Methods on date when ERP decision is made.
- Methods to be drafted into AOAC format by a knowledgeable AOAC staff member or designee in collaboration with the ERP and method author.
- Report of FAOMS decision complete with ERP report regarding decision including scientific background (references etc) to be published concurrently with method in traditional AOAC publication venues.

Method in First Action Status and Transitioning to Final Action Status

- Further data indicative of adequate method reproducibility (between laboratory) performance to be collected. Data may be collected via a collaborative study or by proficiency or other testing data of similar magnitude.
- Two years maximum transition time (additional year(s) if ERP determines a relevant collaborative study or proficiency or other data collection is in progress).
- Method removed from First Action Official Methods and OMA if no evidence of method use available at the end of the transition time.
- Method removed from First Action Official Methods and OMA if no data indicative of adequate method reproducibility is forthcoming as outlined above at the end of the transition time.
- ERP to recommend Method to Official Final Action Status to the OMB.
- OMB decision on First to Final Action Status

Revised October 2013

Online Technical Resources

Method Development, Optimization & Validation

- OMA - Appendix F - Guidelines for Standard Method Performance Requirements
- Homogeneity
- Guide for Writing Methods in AOAC Format
- Statistics Protocol Review Form
- OMA - Appendix D: Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis
- OMA - Appendix G: Procedures and Guidelines for the Use of AOAC Voluntary Consensus Standards to Evaluate Characteristics of a Method of Analysis
- OMA - Appendix I: AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Biological Threat Agent Methods and/or Procedures
- OMA - Appendix J: AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Microbiological Methods for Food and Environmental Surfaces
- OMA - Appendix K: Guidelines for Dietary Supplements and Botanicals
- OMA - Appendix L: AOAC Recommended Guidelines for Stakeholder Panel on Infant Formula and Adult Nutritionals (SPIFAN) Single-Laboratory Validation
- OMA - Appendix M - Validation Procedures for Quantitative Food Allergen ELISA Methods: Community Guidance and Best Practices
- Safety Checklist

Method Review

- Examples of Statistical Analysis
- Statistics Manuscript Review Form
- OMA - Appendix A: Standard Solutions and Reference Materials
- OMA - Appendix D: Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis
- OMA - Appendix H: Probability of Detection (POD) as a Statistical Model for the Validation of Qualitative Methods

Miscellaneous

- Definition of Terms and Explanatory Notes
- OMA - Appendix B: Laboratory Safety
- OMA - Appendix E: Laboratory Quality Assurance
- OMA - Appendix C: Reference Tables

All resources are accessible at
http://www.aoac.org/vmethguidelines.htm

For questions, please contact:
P 301-924-7077 x157 E dmckenzie@aoac.org

About Expert Review Panels (ERPs)

ERP OVERVIEW:

An Expert Review Panel (ERP) is assembled to review and adopt methods as Official First Action. ERPs will track Official Methods for two years or until such time as reproducibility has been demonstrated and cumulative feedback on method use and performance are obtained. ERPs will make a recommendation regarding Final Action method status for all OMAs to the Official Methods Board (OMB).

All ERP members are expected to serve with the highest integrity and without direct or indirect conflicts of interest. A method assignment can last two years. All members of the ERP are expected to actively participate in ERP meetings and to perform duties and reviews in timely fashion. All members should maintain strict adherence to review timelines and deadlines. AOAC staff documents ERP deliberations.

ESTABLISHING AN EXPERT REVIEW PANEL:

- AOAC staff issues a Call for Experts:
  - Based on voluntary consensus standards and methods submitted to AOAC INTERNATIONAL that may meet the standards.
  - Proprietary and sole source method developers submit individual methods to the AOAC Research Institute.
  - Candidates are asked to submit a CV or information that demonstrates expertise to AOAC staff if not already part of a recognized pool of experts.
- AOAC Chief Scientific Officer (CSO) reviews the documentation for the candidates and make recommends a slate for an expert review panel including the chair to the Official Methods Board.
- The candidate list and supporting documentation are forwarded to the Chair of the OMB who will assign the review to at least two OMB members.
- The OMB reviewers will review the candidates for expertise and perceived conflicts of interest and the OMB may then approve the members of the ERP. A Chair for the ERP is also approved.

EXPERT REVIEW PANEL (ERP):

- Review, discuss and demonstrate consensus on methods for Official First Action method status.
- Participate in the publications process of First Action methods.
- Track and discuss feedback all First Action methods for two years.
- Reach and demonstrate consensus on recommendations for Final Action method status.
- Actively participate in the broader stakeholder effort.

ERP CHAIR:

- Lead ERP discussions in the review and adoption of methods for First Action Official Methods.
- Participate in stakeholder panel activities.
- Review and approve ERP report.
- Work with AOAC staff, working groups and other stakeholder panels to ensure a thorough understanding of the standard method performance requirements and the methods to be assessed.
- Implement the OMB First Action to Final Action Guidelines with the ERP members.
- Advise and review First Action methods and post First Action publications.
- Represent the ERP in presenting the ERPs recommendation to the Official Methods Board regarding Final Action method status.

MECHANICS OF AN AOAC EXPERT REVIEW PANEL

- AOAC CSO assigns methods for review to the expert review panel members.
- For each method, 2 ERP members are assigned as primary and secondary reviewers and present at the ERP meeting.
- All members are expected to actively participate and review methods for First Action Official Method status - conducting thorough and prompt review of methods and being prepared to speak on assigned methods at ERP meetings
- The ERP chair and the 2 reviewers for each method are expected to participate in the publications peer review process for First Action methods.
- ERP reviewers track assigned methods that were adopted as First Action Official Methods and update ERP on method use during two year period between First Action and Final Action
  ERP members are expected to participant in the stakeholder panel activities and/or community at large .

- *ERPs can work with topic advisors (aka, subject matter experts)*
- *OMB can recognize a pool of experts from which ERP members can be selected*

Eligibility Criteria for Expert Reviewers

Be a key expert and/or thought leader of the method or priority under consideration.

- Demonstrated knowledge in the appropriate scientific disciplines.
- Demonstrated knowledge regarding data relevant to adequate method performance.
- Demonstrated knowledge of practical application of analytical methods to bona fide diagnostic requirements.

Be approved by the Official Methods Board

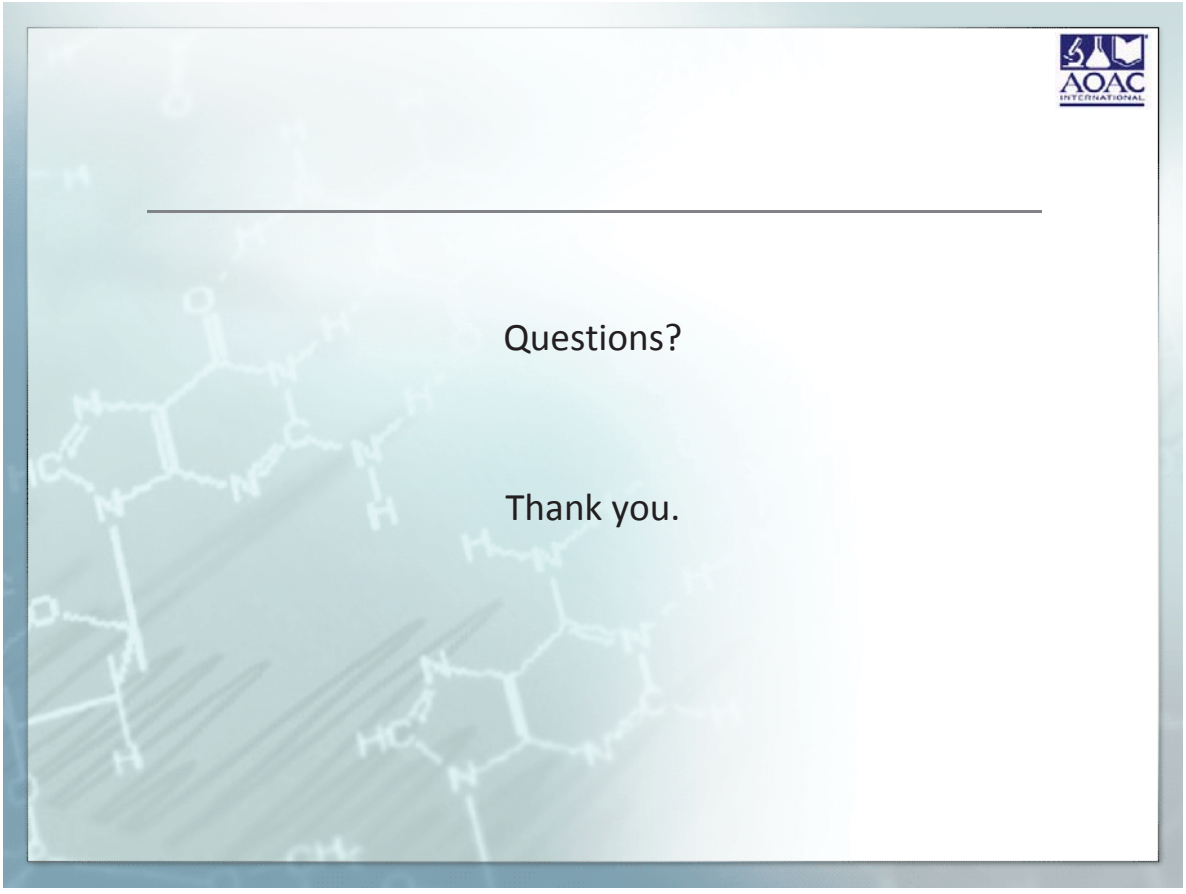
- Qualifications must be clearly described and submitted to AOAC headquarters.

Duties of Expert Reviewers

Members of the Pool of Experts will be called upon to serve on ERPs as needed and to review documents .These documents may include:

- Procedural documents on how methods will be selected and how single laboratory validation studies will be done;
- Methods submitted for consideration as First Action Official Methods;
- Methods submitted for selection for further validation studies;
- Protocols to be used for single laboratory validation studies;
- Selection of methods to be considered for full collaborative studies; and
- Validation study reports

Revised October 2013



The Scientific Association Dedicated to Analytical Excellence®

Stakeholder Panel on Strategic Food Analytical Methods:

Expert Review Panel on Selected Food Allergens

AOAC Candidate Method #ALL-01

Detection and Quantitation of Selected Food Allergens using LCMS/MS: Second Submission

- Author(s): Lee Sun New, Hua-Fen Liu, Andre Schreiber, Vincent Paez
- Submitted by: Andre Schreiber, SCIEX
- Enclosures: 0
- Submitter notes: None

Primary Reviewer: Linda Monaci

Secondary Reviewer: Sneh Bhandari

Additional Submitted Review(s): Tomasz Tuzimski (as of March 8, 2017)

View AOAC SMPR 2016.02

View Candidate Method ALL-01 (ERP Members Only)

AOAC SPDS ERP - Set 3 Review Form 2

Name	Linda Monaci
E-mail	linda.monaci@ispa.cnr.it
Organization	CNR-ISPA
Title of Method	Detection and Quantitation of Selected Food Allergens by LCMS/MS
AOAC Candidate Method Number (e.g. ALN-01)	ALL-01
Applicable SMPR	yes
Summary:	The method described is a LC-MS/MS method for the simultaneous detection of multiple allergens basing on the detection of unique peptide markers for each allergenic food namely egg, milk, peanut and hazelnut along the same LC-MS run. The method has been run on different triple quadrupole MS instrument by building an acquisition method monitoring at least two transitions for each peptide marker targeted. The sensitivity, specificity and applicability of the method has been also investigated in the different food commodities analysed.
I. Review of Method Only	
1. Does the applicability of the method support the applicability of the SMPR? If not, please explain what is missing.	Yes
2. Does the analytical technique(s) used in the method meet the SMPR? If not, please specify how it	Despite the analytical technique that in principle is expected to meet the SMPR requirements, there is still an incorrect way of calculating MQL and MDL. This arises from an erroneous noise estimation and consequently an erroneous calculation of the resulting S/N. Despite the correct approach the authors stick with the use of a

differs from what is stated in the SMPR.	software under AB SCIEX company for the estimation of S/N. According to my experience these kind of software are very much optimistic and will not allow comparability of results obtained on different machines commercialized by different companies. The SMPR reports that the estimation of s0 done in the proper way should lead to reliably calculate the final MQL and MDL.
3. Are the definitions specified in the SMPR used and applied appropriately in the method? If no, please indicate how the terms are used.	Yes for many of them. Still some problems in the correct calculation of MDL and MQL and in the calculation of the recovery that should be done on 7 independent analysis for each concentration level tested (referred to spiked or incurred blank samples) (and not 3 independent analysis for each concentration level as done in this work)
4. Does the method, as written, contain all appropriate precautions and warnings related to the method's reagents, components, instrumentation, or method steps that may be hazardous? If no, please suggest wording or option(s).	Yes
II. Review of Supporting Information	
1. Are the definitions specified in the SMPR used and applied appropriately in the supporting documentation (manuscripts, method studies, etc…)? If not, please explain the differences and if the method is impacted by the difference.	Yes although some confusion appears in the manuscript especially in the chromatograms shown in figures 7, 8, 9, 10. It is never specified if the chromtagramas shown at 0 and 10 ppm levels refer to spiked or incurred food samples….this could make a big difference.

2. Is there information demonstrating that the method meets the SMPR Method Performance Requirements using the Reference Materials stated in the SMPR? If not, then specify what is missing and how this impacts demonstration of performance of the method.	Yes
3. Is there information demonstrating that the method performs within the SMPR Method Performance Requirements table specifications for all analytes in the SMPR applicability statement? If not, please specify what is missing and whether or not the method's applicability should be modified.	Again: the calculation of MDL and MQL is not correct. The calculation should not use a commercial software for the estimation of S/N ratio and consequently final sensitivity of the method. Such approach is not correct and would never apply to other instruments since it is instrument and brand specific. Please carefully check the proper Anal chem guidance for the correct estimation of MDL and MQL. This value should be recalculated and also the recovery according to what stated in the SMPR guidelines (n of independent analyses for each concentration level).
III. General Submission Package	
1. Based on the supporting information, were there any additional steps in the evaluation of the method that indicated the need for any additional precautionary	no

statements in the method?	
2. Is there information demonstrating that the method system suitability tests and controls as specified in the SMPR worked appropriately and as expected? If no, please specify.	yes
3. Based on the supporting information, is the method written clearly and concisely? If no, please specify the needed revisions.	yes
4. Based on the supporting information, what are the pros/strengths of the method?	the pros is the potential of the MS/MS based method to detect along one run several allergens such as egg, milk, hazelnut, peanut with possible inclusion of other nuts according to some preliminary data shown. Also another advantage is the sharp protocol required for sample preparation.
5. Based on the supporting information, what are the cons/weaknesses of the method?	sensitivity of the method should be better investigated and also recovery of the food matrices depending on the type of inclusion done whether spiked or incurred.
6. Any general comments about the method?	The method has been definitely improved and enriched with additional details and info also thanks to other experiments carried out according to what raised by the reviewers. I would approve the method only if calculation of recovery is properly done (also detailing clearly if it refers to the spiked or incurred food samples; and if it is done according to what reported in the guidance namely n=7 independent analysis for each concentration level). Most importantly I would require to calculate in a correct way the MDL and MQL that is a very

	crucial point since it would make this parameter comparable on the different instruments that can be potentially used for such analysis making it independent on the specific company.
IV. Final Recommendation	
Do you recommend this method be adopted as a First Action and published in the Official Methods of Analysis of AOAC INTERNATIONAL? Please specify rationale.	After some few modifications

AOAC SPSFAM ERP REVIEW FORM - MARCH 13, 2017

Submission Date	2017-03-01 19:29:16
Name	SNEH BHANDARI
E-mail	sneh.bhandari@mxns.com
Organization	Silliker Laboratories
Title of Method	Detection and Quantitation of Selected Food Allergens using LC-MS/MS (Revision 2)
AOAC Candidate Method Number (e.g. ALN-01)	ALL-01
Applicable SMPR	2016.002

I. General Summary:

A LC-MS/MS based method for the detection and quantitation of whole egg (egg white and egg yolk), whole milk, peanut butter, and hazelnut commodity in food matrices listed in AOAC SMPR 2016.002 was developed and tested. The method uses triple quadrupole mass spectrometry and Multiple Reaction Monitoring (MRM) of characteristic transitions of precursor ions to fragment ions of a marker peptides to uniquely identify each allergen. The calibration curves were plotted using the ratio of unique peptide peak area of each allergen commodity in food matrix to spiked labeled internal standard (area ratio) against incurred or spiked commodity concentration. The recoveries (%) for each allergen commodity were estimated (n=9). The same quantifier ion was used for the different food matrices except chocolate and wine due to matrix interference or non-specific binding for certain proteins or peptides. The sensitivity and selectivity of the method are demonstrated.. Overall, the method was able to meet the method performance requirements stated in AOAC SMPR 2016.002. For all food matrices, the target commodity analytical range of 10−1000 ppm was achievable and the method demonstrated good repeatability with RSDr < 15% . Except for chocolate, the peptide recoveries ranged from 60.5 to 109.9% in the tested food matrices. The method is able to demonstrate good sensitivity and is able to detect whole egg and the rest of the allergen commodities at a MQL of 3 or 10 ppm, respectively. Similar results were also achieved for the qualifier ion. Except for quantifier ion, poor sensitivity (MQL ≤ 30%) and low recovery (< 60%) were observed for the qualifier ions of milk, peanut and hazelnut in chocolate due to severe matrix effects. The scope of the method is limited to these matrices and allergen commodities.

II. Review of the Method Only:

1. Does the applicability of the method support the applicability of the SMPR? If not, please explain what is missing.	SMPR states detection and quantitation of egg, milk, peanut, and hazelnut food allergens in finished food products and ingredients. The submitted method is able to detect mentioned allergens in selected matrices. Egg white and egg yolk in Cookies, bread, cookie dough, salad dressing and white wine. Whole milk in cookies, infant formula, red wine and dark chocolate. Peanut and hazelnut in cookies, ice cream, breakfast cereals and milk chocolate. The method has not been applied to different varieties of specified matrices in respective allergen category.
2. Does the analytical technique(s) used in the method meet the SMPR? If not, please specify how it differs from what is stated in the SMPR.	Yes.

3. Are the definitions specified in the SMPR used and applied appropriately in the method? If no, please indicate how the terms are used.	Yes.
4. Does the method, as written, contain all appropriate precautions and warnings related to the method's reagents, components, instrumentation, or method steps that may be hazardous? If no, please suggest wording or option(s).	No. Need to be added.
III. Review of Info in Support of Method:	
1. Are the definitions specified in the SMPR used and applied appropriately in the supporting documentation (manuscripts, method studies, etc...)? If not, please explain the differences and if the method is impacted by the difference.	Yes.
2. Is there information demonstrating that the method meets the SMPR Method Performance Requirements using the Reference Materials stated in the SMPR? If not, then specify what is missing and how this impacts demonstration of performance of the method.	Yes, but only for selected matrices and even those have not been repeatable in other samples, for example was applied on cookie type. Will method provide similar results in other cookies without using separate calibration curve. The method requires separate calibration curve for different samples even for the matrices for which the method has been demonstrated to be applicable. Reference materials are used to calibrate the method but not used to establish accuracy of the over all method. Other allergen reference materials may be used to establish accuracy of the method for specified matrices. The method accuracy may be established further.
3. Is there information demonstrating that the method performs within the SMPR Method Performance REquirements table specifications for all analytes in the SMPR applicability statement? If not, please specify what is missing and whether or not the method's applicability should be modified.	Yes but for selected matrices. The method meets SMPR method performance requirements specifications but those have been demonstrated for selected matrices in only single sample for the matrix.
IV. General Submission Package:	
1. Based on the supporting information, were there any additional steps in the evaluation of the method that indicated the need for any additional precautionary statements in the method?	No

2. Is there information demonstrating that the method system suitability tests and controls as specified in the SMPR worked appropriately and as expected? If no, please specify.	Yes
3. Based on the supporting information, is the method written clearly and concisely? If no, please specify the needed revisions.	Yes
4. Based on the supporting information, what are the pros/strengths of the method?	Comprehensive evaluation of the specified marker peptides in selected matrices in selected samples. The concept evaluated is a strong point of the method.
5. Based on the supporting information, what are the cons/weaknesses of the method?	The method has been demonstrated to be applicable to selected matrices. The contents of unique marker peptide is different in even in the same matrix type like cookie thus method may requires separate calibration curve for every sample type even for those matrices where it has been demonstrated to be working. The method has not been demonstrated for its performance in different types of the matrices in scope like Cookie etc.
6. Any general comments about the method?	It's a very good concept but how practical to apply it in field not known. The methods accuracy not established using other reference materials (which have not used to calibrate the method) and by analysis using other established methods for the same samples.

V. Final Recommendation

Do you recommend this method be adopted as a First Action and published in the Official Methods of Analysis of AOAC INTERNATIONAL?	The method may be adopted as a First Action for only matrices for which its performance has been demonstrated satisfactory in the submitted report.

Please specify rationale.

AOAC SPDS ERP – ALL-01 Review

Name	Melanie Downs
E-mail	mdowns2@unl.edu
Organization	University of Nebraska-Lincoln
Title of Method	Detection and Quantification of Selected Food Allergens using LC-MS/MS (Revision 2)
AOAC Candidate Method Number (e.g. ALN-01)	ALL-01
Applicable SMPR	2016.002
Summary:	The method described in the submission can broadly be described as a targeted bottom-up proteomics detection method. The authors used discovery bottom-up proteomics to identify target tryptic peptides from each allergenic food. These target peptides were subsequently incorporated into the final targeted method, using a selected reaction monitoring (SRM) strategy to monitor specific transitions of these peptide targets. The method claims to detect and quantify egg, milk, peanut, and hazelnut in several different matrices. The sample preparation described is consistent with a typical bottom-up proteomics experiment, including protein extraction, reduction, alkylation, trypsin digestion, and sample clean-up. Defatting is also an optional step prior to protein extraction for some matrices. In some instances, internal standard peptides are also added to the peptide digests. The digested samples are subsequently separated by RP-HPLC, inline with ESI-MS/MS analysis by a QTRAP instrument. The pre-established peptide transitions were monitored with a scheduled SRM method over the course of a 12 minute

chromatographic gradient (2-40% acetonitrile).

With respect to how the transition data was processed and analyzed, particularly with respect to the quantitative analysis, some aspects require additional information. The authors seem to recommend quantification by developing a specific calibration curve for each allergenic food target and food matrix combination, using incurred/spiked foods. The quantification calibration curve would utilize a ratio of the spiked/incurred peptide peak area to the peak area of an internal heavy standard peptide spiked in following sample digestion. The concentration in an unknown sample would be determined by including the heavy internal standard peptide prior to analysis, and determining the subsequent light(sample):heavy peak area ratio and comparing that to the calibration curve. What remains unclear is how an end user would implement this calibration curve process in order to conduct the method. Will the end user need to analyze the spiked food calibration curve on their own instrument? If so, will the method developers provide the calibration curve materials? Also, how similar must the calibration curve food matrix be to the unknown sample food matrix? The authors have only shown information about the one set of food matrices that they prepared for the calibration curve itself, not for other food products. It remains quite unclear how an end user would conduct the quantitative analysis. In addition, the authors did not provide much information about how each transition and/or peptide would be evaluated either qualitatively or quantitatively in this system. For example, is the sum of the individual peptide transitions utilized for the peak area calculations? Are both transitions for each peptide required? In addition, it is unclear how many peptides and transitions are actually monitored and quantified in the final method. It is initially stated that two transitions are monitored from two peptides

	originating from two proteins in each allergenic food. However, the quantitative method information seems to indicate that only one peptide from each food is used for quantification (with two corresponding transitions). How are calculations conducted if different peptides disagree on quantification or qualitative presence?
1. Does the applicability of the method support the applicability of the SMPR? If not, please explain what is missing.	Yes
2. Does the analytical technique(s) used in the method meet the SMPR? If not, please specify how it differs from what is stated in the SMPR.	Yes
3. Are the definitions specified in the SMPR used and applied appropriately in the method? If no, please indicate how the terms are used.	No. In several cases the authors appear to use different units than those indicated in the SMPR. Specifically, the authors use whole milk powder instead of whole fluid milk, spray dried whole egg instead of whole liquid egg, and peanut butter instead of peanuts. The differences in these units can result in up to an 8-fold difference in concentration, as is the case with whole milk powder vs. whole fluid milk. In some instances, these differences would result in failure to meet the method performance requirements. For example, the stated MQL of 3 ppm whole milk powder in cookie would equate to approximately 24 ppm whole fluid milk in cookie. In addition, the presentation of separate results for egg white and egg yolk are not in keeping with the SMPR, which calls for the detection and quantification of whole egg.

4. Does the method, as written, contain all appropriate precautions and warnings related to the method's reagents, components, instrumentation, or method steps that may be hazardous? If no, please suggest wording or option(s).	Yes, although more detail may be beneficial. The method instructs users to refer to safety data sheets and local rules for health and environmental safety. Even though the potential hazards associated with this method are similar to other general laboratory procedures, it may be beneficial for an end user to have the hazards identified more specifically (e.g. hazards associated with handling formic acid or hexane and appropriate precautions).
1. Are the definitions specified in the SMPR used and applied appropriately in the supporting documentation (manuscripts, method studies, etc...)? If not, please explain the differences and if the method is impacted by the difference.	No. As stated in previous answer, the use of dried versions of whole milk and whole egg instead of the liquid versions, as defined in the SMPR, cause issues with the subsequent results and measurement units. While the dried versions of the allergenic foods are indeed more suitable to work with (and more relevant to the food industry), they are not what is defined in the SMPR. The authors would at least need to very specifically define any theoretical or empirical conversions between the materials, which they do not appear to have done given the information in the submission.
2. Is there information demonstrating that the method meets the SMPR Method Performance Requirements using the Reference Materials stated in the SMPR? If not, then specify what is missing and how this impacts demonstration of performance of the method.	Yes- for the materials used as calibrants for the method. The authors did not, however, analyze any external incurred reference materials, only those prepared in house. Whether or not the reference materials indicated in the SMPR are relevant for demonstrating performance is somewhat debatable, but as mentioned elsewhere, the authors should demonstrate method performance on samples other than those used to create the calibration curve.
3. Is there information demonstrating that the method performs within	No. The authors should give the actual values for performance requirements such as MDL, MQL, and RSDr, instead of just less than values. It is also

the SMPR Method Performance REquirements table specifications for all analytes in the SMPR applicability statement? If not, please specify what is missing and whether or not the method's applicability should be modified.	unclear from the submission which data were used to generate these values. As noted in previous questions regarding definitions, the use of whole milk powder instead of whole liquid milk and spray dried whole egg instead of liquid whole egg affects the MQL, MDL, and quantitative range values for method performance in some cases. Also, as discussed in the summary and in later questions, there are issues around the clarity of the quantification strategy, which also impacts the method the authors used to determine Recovery performance.
1. Based on the supporting information, were there any additional steps in the evaluation of the method that indicated the need for any additional precautionary statements in the method?	No.
2. Is there information demonstrating that the method system suitability tests and controls as specified in the SMPR worked appropriately and as expected? If no, please specify.	The choice of materials for the system suitability test (fractionated or partially purified versions of proteins from two foods) seems a bit unusual and requires more justification. Also, the levels at which these suitability samples were run does not correspond to the SMPR, which requires blank check samples and check standards at the lowest point and midrange point of the analytical range. Also, it's unclear even how the given peptide peak areas would be obtained for Milk.Protein_2.Peptide_B, as this peptide is from beta-casein (see description in general comments), which is not specifically included in the system suitability test sample.
3. Based on the supporting information, is the method written clearly	No. One of the primary issues is with the quantification strategy. It is unclear from the submission how quantification would be conducted

	and concisely? If no, please specify the needed revisions.	by an end user. The authors appear to be suggesting that the amount of allergen in an unknown sample would be determined by comparing the sample area ratio (sample peptide area/heavy internal standard area) to the calibration curve constructed from the incurred/spiked food area ratio. Is that correct? Would the authors intend for each user to run the incurred/spiked food calibration curve? If so, will those materials be available for end users? Also, if that is the intended quantification method to obtain a result, why did the authors use different quantitative comparisons in their recovery analysis? Lastly, if the quantification strategy uses the incurred/spiked foods as the calibration curve, then the quantitative data shown in the submission only supports the performance of the method with the standard curve itself, not on any sort of unknown or reference samples. In addition, the authors initially show the results for just the one quantifier ion for each allergenic food (Tables 10-14), but then go on to show quantitative results for the qualifier ion in Appendix 4. How were those results based on the qualifier ion calculated? Did the authors also have heavy internal standards for the qualifier ion? The method and the supporting information are also not clear on how the data from the other transitions described as being monitored in the method (from the other peptides and/or proteins) would be assessed. Supposedly two transitions for each of two peptides from two proteins from the allergenic source were monitored, but no data for other transitions/peptides/proteins (aside from the qualifier/quantifier ions) are presented in the supporting information. Does confirmation of presence of the allergenic food require detection of all of the transitions or only some of them?	

4. Based on the supporting information, what are the pros/strengths of the method?	If additional details on how the supporting information were generated are provided, it may be that the method fits a majority (but not all) of the performance requirements. The results generated from the in house incurred/spiked food calibration curve appear to be quite good with respect to repeatability. In the tested food matrices, the method also appears to have the specificity required for a food allergen method.
5. Based on the supporting information, what are the cons/weaknesses of the method?	As discussed elsewhere in this review, the reporting units for the method do not match those in the SMPR, and this issue must be addressed as it affects whether the method meets many of the performance requirements. The quantification strategy that was applied and how an end user would quantify results needs extensive clarification (as discussed in previous questions). If the quantification is to be conducted with a calibration curve derived from the incurred/spiked foods produced by the method developer, then the assessment of method performance must be conducted on other relevant samples.
6. Any general comments about the method?	The authors state (on p. 18) that, “For the final method, two proteins, two unique peptides for each protein and two MRM transitions for each peptide, i.e. total of eight MRM transitions, were used for each allergen commodity to ensure identification confidence (Table 2).” However, this statement does not hold true in several cases: Egg: - The peptides (EggYolk.Protein_2.Peptide_A and EggYolk.Protein_2.Peptide_B) listed in Table 1 as targets for Gal d 5, serum albumin, are not present in this protein. Instead, these peptides are from Vitellogenin-2. The other set of peptides from egg yolk are correctly stated to be from Gal d 6, Vitellogenin-1, which is another isoform of the protein.

- The peptides are, however, shown to be from the correct proteins in Appendix 1.

Milk:
- The authors do indicate two peptides from Bos d 9 (alpha-s1-casein). However, the other two peptides given for milk are from different proteins. Milk.Protein_2.Peptide_A is from Bos d 5 (beta-lactoglobulin) and Milk.Protein_2.Peptide_B is from Bos d 11 (beta-casein). Despite the name given to the peptides, they are not from the same protein.

For milk, the authors therefore have two peptides for one protein and only one peptide for two additional proteins. In the case of the beta-lactoglobulin and beta-casein peptides, there is only one quantifier peptide and one qualifier peptide between these two proteins.

- Again, the peptides are, shown to be from the correct proteins in Appendix 1.

In addition, while the authors state that a total of eight MRM transitions for each allergen commodity are used in the method, validation seems to have only been conducted for one peptide (two transitions) for each commodity-matrix combination. What happens when the quantifier ion is detected but the qualifier ion(s) is/are not?

It is unclear from the description of the preparation of the incurred/spiked foods whether all of the target allergenic foods (milk, egg, peanut, and hazelnut) were incurred/spiked into the same batch of the food matrix (e.g. cookie) or whether each allergenic food was incurred into separate batches of the food matrices.

The authors also do not consistently and clearly state all units. Due to the differences in potential differences, all units must be complete and specific,

	i.e. “ppm whole milk powder” or “ppm whole fluid milk”, not simply “ppm milk”. The authors also indicate that three laboratories performed the method but it is unclear how these data from different labs are presented in the tables/results given.
Do you recommend this method be adopted as a First Action and published in the Official Methods of Analysis of AOAC INTERNATIONAL? Please specify rationale.	No. Due to the issues outlined in this review, particularly with respect to the differences in results units and the need for clarification of the quantification strategy for the end user, there are still substantial revisions that are needed. In addition, the submission contains some critical errors (e.g. incorrect assignment of peptides to proteins) that need to be corrected. Some of the other aspects of how the data are processed, analyzed, and interpreted also require further clarification before the method could be properly reviewed or implemented by an end user.

AOAC SPSFAM ERP REVIEW FORM - MARCH 13, 2017

Submission Date	2017-02-28 12:44:08
Name	Tomasz Tuzimski
E-mail	tomasz.tuzimski@umlub.pl
Organization	Medical University in Lublin, Poland
Title of Method	Detection and Quantitation of Selected Food Allergens using LC-MS/MS (Revision 2)
AOAC Candidate Method Number (e.g. ALN-01)	ALL-01 (Revision 2)
Applicable SMPR	2016.002

I. General Summary:

The proposed method entitled 'Detection and Quantitation of Selected Food Allergens using LC-MS/MS (Revision 2)' described by Lee Sun New, Andre Schreiber and Hua-Fen Liu is applicable for the detection and quantitation of egg, milk, peanut, and hazelnut food allergens in finished food products and ingredients by LC-MS/MS.
The method uses triple quadrupole mass spectrometry and selective Multiple Reaction Monitoring (MRM) of characteristic transitions of precursor ions to fragment ions of multiple proteins and peptides to uniquely identify each allergen. Characteristic signature peptides were chosen for each alergen, and MRM transitions for each signature peptide were determined based on their uniqueness compared to background proteins and their sensitivity of detection. For each allergen multiple unique peptides were chosen from unique proteins, and two MRM transitions per peptide were chosen.
The method performance requirements were met for the detection of egg, milk, peanut and hazelnut in a number of food matrices.
The method can be easily extended to the detection of other allergens, including soy and other tree nuts (almonds, Brazil nut, cashew, pine nut, pistachio, pecan, and walnut). The method was verified in-house and across two other different laboratories.

II. Review of the Method Only:

1 Does the applicability of the method support the applicability of the SMPR? If not, please explain what is missing.	YES: The applicability of the method is adequate to the applicability of the SMPR. The target commodity analytical range of 10–1000 ppm for all matrices with recoveries (refer to Definitions) between 60–120% and RSDr of less than 20% were achieved for all allergen commodities in the food matrices required for AOAC SMPR 2016.002.
2. Does the analytical technique(s) used in the method meet the SMPR? If not, please specify how it differs from what is stated in the SMPR.	YES: The analytical techniques in the method are adequate and meet the SMPR.
3. Are the definitions specified in the SMPR used and applied appropriately in the method? If no, please indicate how the terms are used.	YES: Definitions, which are specified in the SMPR, were listed in the description, also were applied appropriately in the method.

4. Does the method, as written, contain all appropriate precautions and warnings related to the method's reagents, components, instrumentation, or method steps that may be hazardous? If no, please suggest wording or option(s).	Yes: The method contains all appropriate precautions and warnings related to the method's reagents, components, instrumentation, or method steps that may be hazardous.
III. Review of Info in Support of Method: **1. Are the definitions specified in the SMPR used and applied appropriately in the supporting documentation (manuscripts, method studies, etc...)? If not, please explain the differences and if the method is impacted by the difference.**	YES: The definitions specified in the SMPR were used and applied appropriately in the supporting documentation (manuscripts, method studies, etc.).
2. Is there information demonstrating that the method meets the SMPR Method Performance Requirements using the Reference Materials stated in the SMPR? If not, then specify what is missing and how this impacts demonstration of performance of the method.	YES: There are information demonstrating that the method meets the SMPR Method Performance Requirements using the Reference Material stated in the SMPR.
3. Is there information demonstrating that the method performs within the SMPR Method Performance REquirements table specifications for all analytes in the SMPR applicability statement? If not, please specify what is missing and whether or not the method's applicability should be modified.	YES: There are information demonstrating that the method performs within the SMPR Method Performance Requirements table specifications for all analytes in the SPMR applicability statement.
IV. General Submission Package: **1. Based on the supporting information, were there any additional steps in the evaluation of the method that indicated the need for any additional precautionary statements in the method?**	In my opinion, there is no need to implement any additional steps in the method evaluated.

2. Is there information demonstrating that the method system suitability tests and controls as specified in the SMPR worked appropriately and as expected? If no, please specify.	YES: There are information demonstrating that the method system suitability tests and control as specified in the SMPR worked appropriately and expected.
3. Based on the supporting information, is the method written clearly and concisely? If no, please specify the needed revisions.	The method is well described and substantively prepared. The project of the method is well integrated and includes a clear and concise description.
4. Based on the supporting information, what are the pros/strengths of the method?	The developed method was evaluated following the definitions of AOAC SMPR 2016.002 with respect to Method quantitation limit (MQL), Method detection limit (MDL), Linearity, Repeatability, Reproducibility, Recovery. Specificity is another important analytical parameter. Characteristic signature peptides were chosen for each allergen, and MRM transitions for each signature peptide were determined based on their uniqueness compared to background proteins and their sensitivity of detection.
5. Based on the supporting information, what are the cons/weaknesses of the method?	Page 49, Table (iv) Hazelnut commodity: For 10 ppm (10000 ppb), information is given that analyte concentrations are BQL (below method quantification limit). Does the procedure fulfil the method criteria? The cons/weakness of the method may be costs. But I think it is inevitable.
6. Any general comments about the method?	Page 42, Table 9: Despite the fact that mean values of SD and RSD% are less than 16.7%, recovery values, as well as SD and RSD%, ought to be provided for all three spiking levels of 10, 100 and 1000 ppm separately.

V. Final Recommendation

Do you recommend this method be adopted as a First Action and published in the Official Methods of Analysis of AOAC INTERNATIONAL? Please specify rationale.	In my opinion, the Method #ALL-01 entitled: Detection and Quantitation of Selected Food Allergens using LC-MS/MS (Revision 2) described by Lee Sun New, Andre Schreiber and Hua-Fen Liu is applicable for the detection and quantitation of egg, milk, peanut, and hazelnut food allergens in finished food products and ingredients by LC-MS/MS. The revised (January 2017) Method #ALL-01 should be adopted in its present form as a First Action and recommended for publication in the Official Methods of Analysis of AOAC INTERNATIONAL.

AOAC SPSFAM ERP REVIEW FORM - MARCH 13, 2017

Submission Date	2017-03-10 07:06:13
Name	SUDHAKAR yadlapalli
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Organization	First source labotatory solutions LLP
Title of Method	Detetcion and quantitation of Selected Food Allergens using LC-MS/,MS
AOAC Candidate Method Number (e.g. ALN-01)	ALL-01 (revision 2)
Applicable SMPR	AOAC SMPR 2016.002

I. General Summary:

Selected Food Allergens are defatted and extracted for proteins. Proteins are digested into peptides and peptides are separated by LC and quantified by using LCMSMS.

II. Review of Method Only:

1. Does the applicability of the method support the applicability of the SMPR? If not, please explain what is missing.	YES
2. Does the analytical technique(s) used in the method meet the SMPR? If not, please specify how it differs from what is stated in the SMPR.	YES
3. Are the definitions specified in the SMPR used and applied appropriately in the method? If no, please indicate how the terms are used.	YES
4. Does the method, as written, contain all appropriate precautions and warnings related to the method's reagents, components, instrumentation, or method steps that may be hazardous? If no, please suggest wording or option(s).	YES

III. Review of Info in Support of Method:

1. Are the definitions specified in the SMPR used and applied appropriately in the supporting documentation (manuscripts, method studies, etc...)? If not, please explain the differences and if the method is impacted by the difference.	YES

2. Is there information demonstrating that the method meets the SMPR Method Performance Requirements using the Reference Materials stated in the SMPR? If not, then specify what is missing and how this impacts demonstration of performance of the method.	YES
3. Is there information demonstrating that the method performs within the SMPR Method Performance REquirements table specifications for all analytes in the SMPR applicability statement? If not, please specify what is missing and whether or not the method's applicability should be modified.	YES

IV. General Submission Package:

1. Based on the supporting information, were there any additional steps in the evaluation of the method that indicated the need for any additional precautionary statements in the method?	YES, Internal standards should be added prior to the extraction to understand the actual recoveries of analytes in sample matrices.
2. Is there information demonstrating that the method system suitability tests and controls as specified in the SMPR worked appropriately and as expected? If no, please specify.	YES
3. Based on the supporting information, is the method written clearly and concisely? If no, please specify the needed revisions.	YES however SRM results must be reported.
4. Based on the supporting information, what are the pros/strengths of the method?	1.Most confirmative method as it is MRM method with eight transitions per allergen. 2. Used SRMs and labeled standards 3. Linearity studies conducted as per SMPR.

5. Based on the supporting information, what are the cons/weaknesses of the method?	Internal standards need to be used prior extraction rather than post extraction.
6. Any general comments about the method?	method may be crosschecked with other equivalent make of instrument to confirm the robustness of the method

V. Final Recommendation

Do you recommend this method be adopted as a First Action and published in the Official Methods of Analysis of AOAC INTERNATIONAL? Please specify rationale.	Yes however thorough recovery studies shall be performed by using addition of internal standards prior to the extraction . SRM need to be verified and reported against actual values.

STAKEHOLDER PANEL ON STRATEGIC FOOD ANALYTICAL METHODS (SPSFAM):

EXPERT REVIEW PANEL (ERP) FOR SELECTED FOOD ALLERGENS

OFFICIAL CHAIR'S EXPERT REVIEW PANEL REPORT

ACKNOWLEDGMENT

The undersigned Chair hereby confirms that the following document has been reviewed and constitutes the final revised version of the Official Chair's Report for the SPSFAM Selected Food Allergens Expert Review Panel held on September 19, 2016.

John Szpylka 27 October 2016

JOHN SZPYLKA, SPSFAM FOOD ALLERGENS ERP CHAIRMAN

STAKEHOLDER PANEL ON STRATEGIC FOOD ANALYTICAL METHODS

EXPERT REVIEW PANEL ON SELECTED FOOD ALLERGENS

METHODS FOR CONSIDERATION:

Conclusion: The Expert Review Panels reviewed two (2) Allergens methods, which were submitted in response to the Call for Methods.

Methods Reviewed: Each method collected by AOAC for consideration by this ERP was assigned a set of reviewers. Methods reviewed included:

- **ALL-01: Detection and Quantitation of Selected Food Allergens Using LCMS/MS**
  - Author(s): Lee Sun New, Hua-Fen Liu, Andre Schreiber, Vincent Paez
  - Submitted by: Andre Schreiber, SCIEX

- **ALL-02: Multiplexed LC-MS Method for the Detection and Quantitation of Selected Food Allergens (milk, hazelnut, peanut and whole egg)**
  - Author(s): Jennifer Sealey Voyksner, Jerry Zweigenbaum and Robert Voyksner
  - Submitted by: Jennifer Sealey Voyksner, ImmunogenX

All methods were reviewed against AOAC SMPR 2016.002, *Standard Method Performance Requirements (SMPRs®) for Detection and Quantitation of Selected Food Allergens.* The decisions of the September 19, 2016 ERP are shown below.

FOOD ALLERGENS ERP MEETING – SEPTEMBER 19, 2016	
Allergens ERP Members Present:	**Allergens ERP Members Absent:**
John Szpylka, Mérieux NutriSciences Sneh Bhandari, Mérieux Nutrisciences Francois Bourdichon, Danone France Cho, Maxxam Analytics Melanie Downs, University of Nebraska – Lincoln Stefan Ehling, Abbott Nutrition Michael Farrow, Abbott Nutrition John Lawry, Covance Linda Monaci, CNR Yasutaka Nishiyama, NH Foods, Ltd. Bert Popping, Mérieux Nutrisciences Tomasz Tumimski, Medical University in Lublin Suhdahar Yadlapalli, First Source Laboratory Solutions LLP Jerry Zweigenbaum, Agilent Technologies	David Almy, Neogen Ken Davenport, 3M Minh Hai Nguyen, Thanglong Instruments Susanne Siebeneicher, R-Biopharm

Observers: Brad Barrett, Gerstel; Julien Brazeall, CFIA; Bob Clifford, Shimadzu; John Deaton, Deerland Enzymes; Carmen Diaz-Amigo, Consultant; Guenther Faffler, Eurofins; Christophe Fuerer, Nestlé; Ali Geffen, DOTS; Steven Gendel, IEM Labs; Thomas Hektor, R-Biopharm; Greg Hostettler, Perrigo; Greg Jaudzems, Nestlé; Jasmin Kraus, Romer Labs; Scott Krepich, Phenomenex; Huafen Liu, SCIEX; Abdul Mabud, TTB; Mary McBride, Agilent; Armen Mirzoian, TTB; Naoki Morishita, NH Foods; Greg Noonan, FDA; Vincent Paez, SCIEX; Shang Jing Pan, Abbott; Scott Radcliffe, Romer Labs; Robert Sheridan, NYS Dept. of Agriculture; Rob Sherlock, DTS\Allergen Bureau; Darsa Siantar, TTB; Amanda Simon, Neogen; Steve Taylor, University of Nebraska; Martine van Gool, FrieslandCampina; Jennifer Voyksner, ImmunogenX; Jinchaun Yang, Waters

AOAC Staff: Scott Coates, Christopher Dent, Dawn Frazier, Deborah McKenzie

Selected Food Allergens Method Reviews and Decisions

AOAC Method #	Manuscript Title, Submitter and Reviewer	ERP Decisions	Consensus	Decision Date
ALL-01	**Title:** Detection and Quantitation of Selected Food Allergens Using LCMS/MS **Submitted by:** Andre Schreiber, SCIEX **Primary Reviewer:** Linda Monaci, CRN Italy **Secondary Reviewer:** Sneh Bhandari, Mérieux Nutrisciences	**The ERP agreed NOT to move this method to First Action *Official Methods of Analysis* Status.** **First Action requirements:** 1. Provide details on the materials used to generate calibration curves. 2. Provide details on generating the cross calibration curves – specifically concentration levels, number of replicates, linearity, and chromatographic responses. 3. Provide more information about how %recoveries were estimated (including spiking agents, spike levels, calculations). 4. Describe use of a Certified Reference Material. 5. Use of internal standard is strongly recommended. 6. Provide additional information of the uniqueness of the selected peptides to ensure no cross-reactivity. 7. Was more than one transition used in this study? 8. Define system suitability requirements. 9. Describe the manner where the measured peptide can be correlated to the concentration of the corresponding commodity. 10. Describe how the LOQ was determined, and if confirmed using a second transition in MDL and MQL. 11. Supply data to support the stated analytical range.	**MOTION** not to move ALL-01 to First Action *Official Methods of Analysis* Status (Monaci/Yadlapalli) 11 in favor, 0 opposed, 2 abstentions. **Motion passed.** **MOTION** to accept the Final Action Requirements for ALL-01 (Valley / Stryffeler) 11 in favor, 0 opposed, 2 abstentions. **Motion passed.**	**09/19/2016**
ALL-02	**Title:** Multiplexed LC-MS Method for the Detection and Quantitation of Selected	**The ERP agreed not to move this method to First Action *Official Methods of Analysis* Status.**	**MOTION** not to move ALL-02 to First Action *Official Methods of Analysis* (Downs /	**09/19/2016**

	Food Allergens (milk, hazelnut, peanut and whole egg) **Submitted by:** Jennifer Voyksner, ImmunogenX **Primary Reviewer:** Melanie Downs, University of Nebraska - Lincoln **Secondary Reviewer:** Tomasz Tuzimski, Medical University in Lublin, Poland	**First Action Requirements:** 1. It is believed the used sample size should be larger to best represent bulk material and to allow accurate quantitation. Is this possible? 2. Supply details/clarification on how the calibration curves were generated. 3. Supply protocol details on the spike allergen vs. extract studies. 4. Describe sample preparation optimization. 5. Clarification of performance of the final method, with associated validation data 6. More information is needed on peptide specificity. 7. More clarification is needed on the extracting conditions using multiple enzymes. 8. Clarify the conversion factors used to express results. 9. Define what is being measured in the CRM. 10. Stronger extraction conditions may be necessary.	Yadlapalli). 10 in favor, 0 opposed, 3 abstentions. **Motion passed.** **MOTION** to accept the First Action Requirements for ALL-02 (Bhandari/Cho). 10 in favor, 0 opposed, 3 abstentions. **Motion passed**.	

Action Items: AOAC staff to work with method authors regarding a follow up ERP.

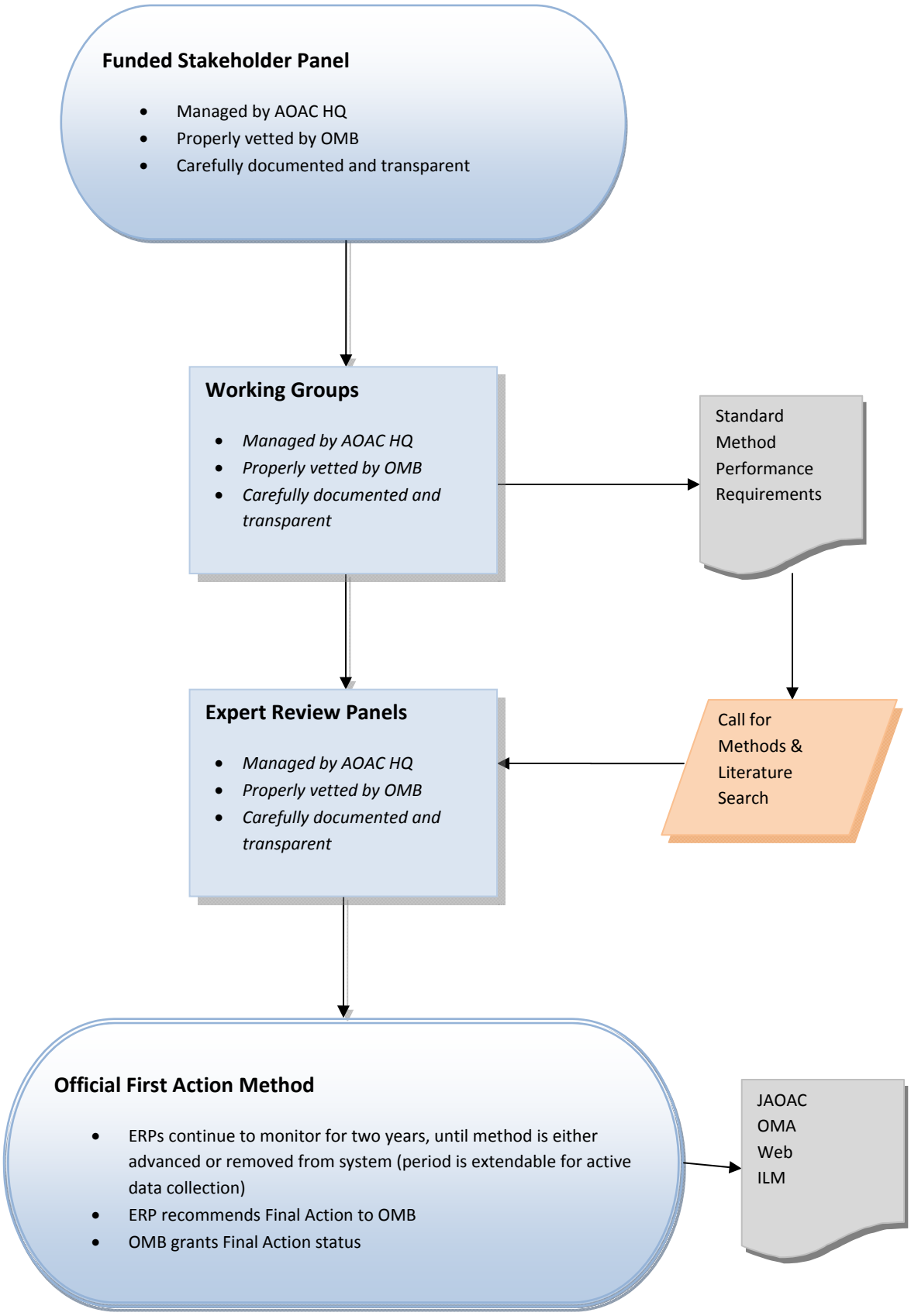
AOAC INTERNATIONAL

First Action Official Methods of Analysis[SM]

Guidance Documents

I. Process Flowchart
II. Process Guidelines
III. Expert Review Panel – Policies & Procedures

Alternate Pathway to Official First Action Method Status



Updated 2011-5-11

AOAC INTERNATIONAL (updated 2011-05-11 by APOFAMS Task Force)

ALTERNATIVE PATHWAY to OFFICIAL FIRST ACTION METHOD STATUS REQUIREMENTS

Expert Review Panels

-Must be supported by relevant stakeholders.

-Constituted solely for the ERP purpose, not for Standard Method Performance Requirements (SMPR) purposes or as an extension of an SMPR.

-Consist of a minimum of seven members representing balance of key stakeholders.

-ERP constituency must be approved by the Official Methods Board (OMB).

-Holds transparent public meetings only.

-Remains in force as long as method in First Action Status.

Official First Action Method Status decision

-Must be made by an ERP constituted or reinstated post 2011-03-28 for Official First Action Status Method Approval (OFASMA).

-Must be made by an ERP vetted for OFASMA purposes by OMB post 2011-03-28.

-Method adopted by ERP must perform adequately against the SMPR set forth by the stakeholders.

-Method must be adopted by unanimous decision of ERP on first ballot, If not unanimous, negative votes must delineate scientific reasons.

-Negative voter(s) can be overridden by 2/3 of non-negative voting ERP members after due consideration

-Method becomes Official First Action on date when ERP decision is made.

-Methods to be drafted into AOAC format by a knowledgeable AOAC staff member or designee in collaboration with the ERP and method author.

-Report of OFAMS decision complete with ERP report regarding decision including scientific background (references etc) to be published concurrently with method in traditional AOAC publication venues.

Method in First Action Status and Transitioning to Final Action Status

-Further data indicative of adequate method reproducibility (between laboratory) performance to be collected. Data may be collected via a collaborative study or by proficiency or other testing data of similar magnitude.

-Two years maximum transition time (additional year(s) if ERP determines a relevant collaborative study or proficiency or other data collection is in progress).

-Method removed from Official First Action and OMA if no evidence of method use available at the end of the transition time.

-Method removed from Official First Action and OMA if no data indicative of adequate method reproducibility is forthcoming as outlined above at the end of the transition time.

-ERP to recommend Method to Official Final Action Status to the OMB.

-OMB decision on First to Final Action Status

EXPERT REVIEW PANELS

--Policies and Procedures—

Introduction

Expert Review Panels (ERP) are created to provide stakeholders with an expert resource to evaluate analytical solutions to identified needs and concerns.

The ERP will be tasked to search for appropriate methods, issue a "Call for Methods" in the ILM and other avenues, and critically evaluate all collected methods. The ERP will then recommend appropriate methods (as submitted or modified) for adoption as Official First Action methods or for further validation. The ERP, if requested by the Committee/Topic Advisor, would be expected to assist in identifying appropriate materials to be used in the validation studies and in reviewing the protocols for such studies.

Outline of ERP establishment process

An Expert Review Panel is established as follows: A stakeholder or stakeholder body submits a request for the creation of an ERP to the AOAC staff. The request includes a description of the subject area, the desired outcome, and should include a list of recommended subject experts with supporting documentation (see "Qualifications of Expert Reviewers"). Included with this list of recommended subject experts could be a recommendation for an ERP Chair. The request is forwarded to the appropriate AOAC Chief Science Officer (CSO) who identifies potential members for the ERP from a recognized Pool of Experts, a Call for Experts on the AOAC website, and from the stakeholder recommendations. The candidate list and supporting documentation are forwarded to the Chair of the OMB who will assign the review to at least two OMB members. The OMB reviewers will review the candidates for expertise and perceived conflicts of interest and the OMB may then approve the members of the ERP. A Chair for the ERP is also selected. The Chair of the ERP will organize meetings of the ERP to discuss and make recommendations relative to method recommendations, the method(s) to be further validated, and the materials to be used in the validation studies. The conclusions and recommendations of the ERP will be transmitted by the ERP Chair to the OMB and stakeholder body. The stakeholder body will proceed with implementation of the ERP's recommendations by organizing the appropriate SLV study and other items needed for application.

Pool of Potential Expert Reviewers:

Candidates for ERPs are pulled from the following sources. Upon acceptance of the request for the formation of an ERP, a Call for Experts is posted on the AOAC website for a minimum of two weeks. Candidates can then contact AOAC with their interest and credentials. Also, AOAC maintains a Pool of Experts database containing a list of

Approved by Official Methods Board, November 13, 2008
Approved by AOAC Board of Directors, December 9, 2008
Appeals Process Appended – September 2009
Revisedby AOAC Board of Directors, May 25, 2011

AOAC members willing to serve as experts and cataloging their education, experience, and other applicable credentials. Candidates can also be recommended by the stakeholder(s). Note: Candidates (except for the chair) do not need to be members of AOAC. The appointment of experts to an ERP will be for a minimum of 3 years.

Qualification of Expert Reviewers: To qualify as an Expert Reviewer, the candidate must meet one of the following requirements: (1) Demonstrated knowledge in the appropriate scientific disciplines. (2) Demonstrated knowledge regarding data relevant to adequate method performance. (3) Demonstrated knowledge of practical application of analytical methods to bona fide diagnostic requirements. These qualifications must be clearly described in a CV submitted to the CSO and kept on file at AOAC headquarters.

Duties: Members of the Pool of Experts will be called upon to serve on ERPs as needed, and to review documents prepared in the course of the project. These documents may include: (1) procedural documents on how methods will be selected and how single laboratory validation studies will be done; (2) methods submitted for consideration as Official First Action Methods; (3) methods submitted for selection for further validation studies; (4) protocols to be used for single laboratory validation studies; (5) the selection of methods to be considered for full collaborative studies; and (6) validation study reports.

Expert Review Panel:

The CSO selects candidates for an ERP from the Pool of Experts database, the Call for Experts on the AOAC website, and from candidates recommended by the stakeholders. Selection of ERP candidates is based upon their knowledge and experience to adequately evaluate the scope of the study and the anticipated number of submitted methods. The size of the ERP will be sufficient to assure the necessary expertise is present. The CSO may recommend one of the Panel members to serve as Chair.

The CSO submits the following to the OMB Chair: The original submission package, a list of all candidates considered for inclusion on the ERP, the slate of recommended candidates, and a list of possible alternates. Explanations for the ERP choices may be included by either the CSO or a stakeholder if desired. The OMB Chair will delegate two members of the OMB to perform a review. The reviewers submit their recommendations in writing to the OMB. The OMB then votes on the reviewers' recommendations. This vote can be either by email or during an OMB meeting. The OMB may choose not to select one or more individuals on the Panel as submitted and may or may not accept the recommendation of the CSO for the panel Chair. A majority of those voting will be required for approval. The vote of the Chair will break any tie. The CSO, ERP members, and stakeholder body are notified of the vote within one week.

Conflict of Interest: It is incumbent upon each ERP member to avoid any known or potential conflicts of interest and make these known to the CSO and OMB Chair. Each pool member chosen for an ERP will be asked to agree to the AOAC Policies and Procedures on Conflicts of Interest evidenced by completing a Conflict of Interest Form.

If a Pool member being considered to serve on any particular panel is an author, or his/her laboratory is the source of a method under consideration by the Panel, they must so indicate to the CSO or OMB Chair. At the discretion of the CSO or OMB, the names of such Pool members may be removed from consideration, or they may be considered to serve on the ERP with the understanding that a deliberate effort will be required to avoid any known or potential conflicts of interest. In these latter cases, assignments of individual methods for peer review will be made in such a way by the Chair that ERP members will not review any method for which they are an author or co-author, or for which their laboratory is the source; and, most importantly, the Chair will require that they abstain from voting on such a method during the final method selection process. The CSO or OMB may also allow Pool members that qualify under the requirements of expert reviewers, but for whom there is a known or potential conflict of interest to be present as an observer on any particular Panel. In these cases, and only at the discretion of the Chair, observers may provide comments, but only if and when called upon by the Chair to do so.

Non-disclosure Statement: All members of an ERP must have signed the AOAC Volunteer Acceptance Form. For certain contracts, each Pool member or observer chosen may be asked to sign a non-disclosure statement agreeing not to discuss or disclose confidential information presented and discussed during meetings of the ERP.

Meetings of the ERP: The ERP Chair will organize meetings of the ERP, to review the methods and accompanying validation data, score them numerically, and prepare a summary report. Meetings of the ERP can include voting members of the Panel, and non-voting members (AOAC staff, stakeholder members, and observers).

The CSO may assist the Panel Chair in facilitating meetings. The members of the Panel are to review distributed documents before the meeting. To facilitate the process, the Chair may assign primary and secondary reviewers for each method. The primary and secondary reviewers prepare a short critique of the method that is distributed or presented to the ERP. If both the primary and secondary reviewers conclude that the method should not be considered further, the ERP Chair may call for a vote by the Panel; if a unanimous vote to drop a method without further discussion results, the Chair removes the method from further consideration. The Panel then discusses each of the remaining methods in turn.

Method Selection Process: The ERP will evaluate all of the methods in a scientifically unbiased manner.

Occasionally, a large number of analytical methods of variable quality are encountered. When this occurs, the following “pre-screening” procedure is suggested to eliminate methods that are not satisfactory. The Chair of the ERP with the assistance of at least one other member of the ERP may review all of the methods and remove unsatisfactory methods from consideration. The remainder of the methods would be sent to the ERP members for review.

The basic requirements for selection of methods for further validation studies will be: fitness for purpose, applicability to the scope needed, clarity of method description, satisfactory performance characteristics, and single laboratory validation data. To assist the Panel, the AOAC will provide a "Methods Selection Worksheet," which may be modified at the discretion of the ERP. ERP members will identify the best method(s) for further validation, and identify any modifications to be made to the method. An example of the Method Selection Worksheet is attached.

Samples: The ERP will be asked to recommend the specific materials (matrices) to be included in the subsequent validation studies, along with detailed justifications.

Summary Report: The Chair of the ERP prepares a Summary Report clearly enunciating the recommendations of the Panel, the manner in which these conclusions were reached, any modifications of the method(s) chosen, and the materials (matrices) to be included in the validation studies. The report is to be submitted to the ERP in a timely fashion after the concluding ERP meeting. Comments are also due back to the ERP Chair in a timely fashion. The report is then sent to the stakeholders and a copy is forwarded to the Chair of the OMB.

Post-ERP Activities: AOAC retains the right to call on the panelists, as well as members of the Industry Groups, for continued assistance in the subsequent validation studies. This may include (1) help in obtaining the required samples for use in the subsequent validation studies, as well as participating laboratories; (2) help in developing and reviewing the validation study protocols; and (3) help in reviewing the data resulting from the validation studies and reviewing the manuscript describing the results. These activities will be coordinated by the CSO.

Method Selection Worksheet

Method Title:
Method Number:

Overall evaluation score (1being lowest, 10 being highest):

Additional Factors to Consider:

Recommendation:

Signature (date):

Expert Review Panel Selection Criteria:

1. AOAC paid consultants and AOAC staff should not act as Chairs of ERPs.

2. Members of the BoD may act as voting members but it is recommended that they sit as non-voting members of the panel, unless the CSO can demonstrate that there are so few experts in the field available to the community that they are needed to move the project forward.

3. Paid consultants of AOAC and AOAC staff may not serve as voting members on ERPs.

4. If a single business location is represented by more than one person on an ERP, that location shall have only one vote.

5. The Chair of the ERP must be a member of AOAC INTERNATIONAL.

Appeals Process:

ERP - Openness of Process and Appeals:

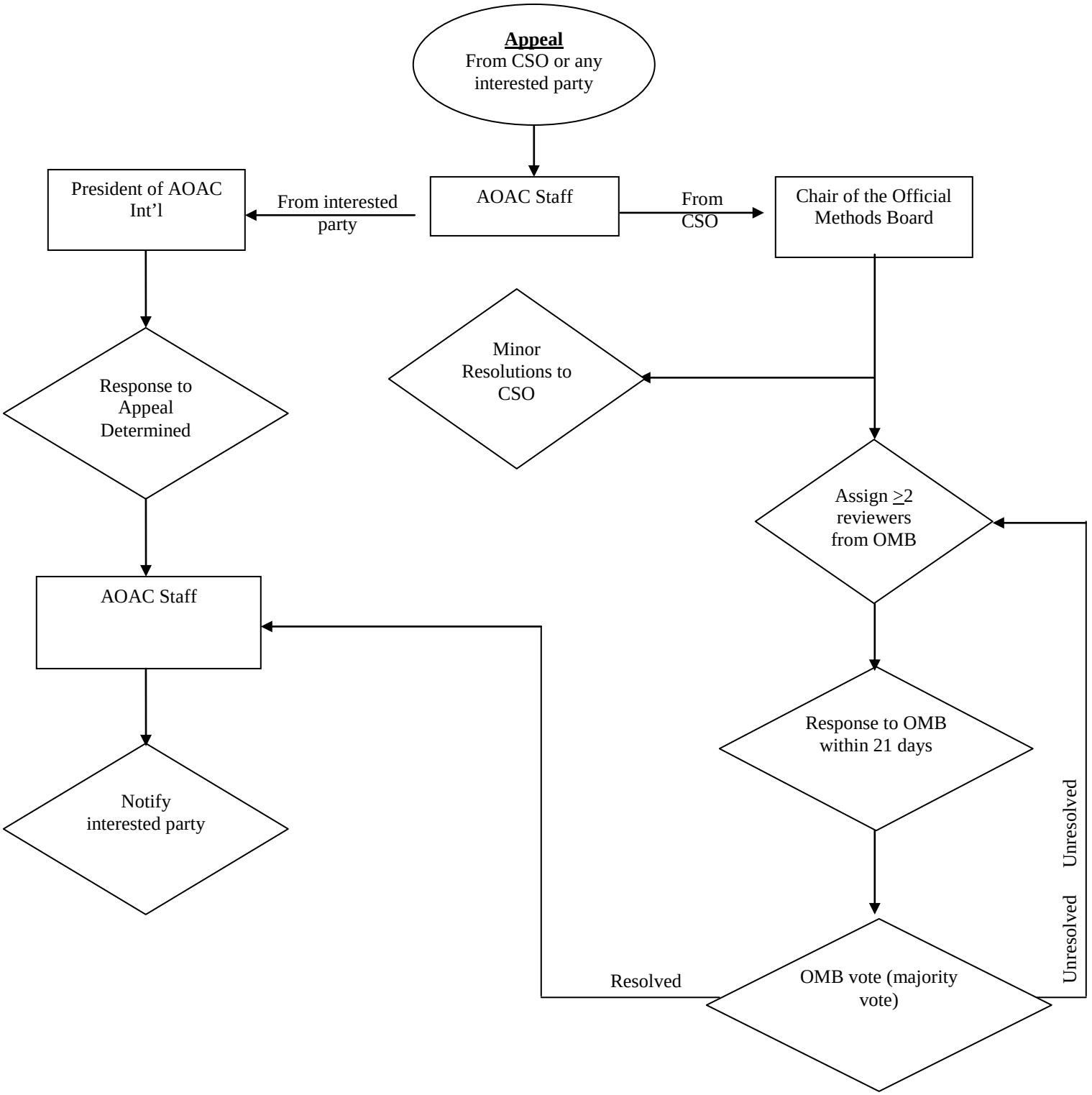
The entire ERP review process is fully open. Any interested party (person, agency, organization, association, company, Chief Scientific Officer (CSO), or group) shall have the right to comment.

Appeals or comments are sent to the AOAC Staff.

Technical decisions by the ERP are final and are not subject to review or appeal. Other questions or issues regarding procedures, conflict of interest, or impropriety may be appealed to the President of the AOAC INTERNATIONAL.

All written concerns will be considered and given a response.

If there is disagreement between the CSO and the Official Methods Board reviewers, the CSO may appeal to the Chair of the Official Methods Board for consideration. The Official Methods Board can select an impartial panel to review the issue, which must report to the Official Methods Board with a resolution within 21 days of its assignment.



Approved by Official Methods Board, November 13, 2008
Approved by AOAC Board of Directors, December 9, 2008
Appeals Process Appended – September 2009
Revisedby AOAC Board of Directors, May 25, 2011

Appendix G: Procedures and Guidelines for the Use of AOAC Voluntary Consensus Standards to Evaluate Characteristics of a Method of Analysis

Expert Review Panels, Official Methods Board, First and Final Action *Official Methods*℠

In early 2011, an AOAC Presidential Task Force recommended that AOAC use Expert review panels (ERPs) to assess candidate methods against standard method performance requirements (SMPRs) to ensure that adopted First Action Official Methods℠ are fit for purpose.

Formation of an ERP

AOAC ERPs are authorized to adopt candidate methods as First Action *Official Methods* and to recommend adoption of these methods to Final Action *Official Methods* status. Scientists are recruited to serve on ERPs by a variety of ways. Normally, a call for experts is published at the same time as a call for methods is posted. Interested scientists are invited to submit their *curriculum vitae* (CV) for consideration. Advisory panel, stakeholder panel, and working group members may make recommendations to AOAC for ERP members. All CVs are reviewed and evaluated for expertise by the AOAC Chief Scientific Officer (CSO). The CVs and CSO evaluations are forwarded to the OMB for formal review. Both the CSO and OMB strive to ensure that the composition of a proposed ERP is both qualified and represent the various stakeholder groups. The recommended ERP members are submitted to the AOAC president who then appoints the ERP members.

Review of Methods

Methods submitted to AOAC in response to a call for methods are collected and compiled by AOAC staff. The AOAC CSO and working group chair perform a preliminary review of the methods and classify them into three categories: (*1*) fully developed and written methods that appear to meet SMPRs; (*2*) fully developed and written methods that may or may not meet SMPRs; and (*3*) incomplete methods with no performance data. Method submitters are apprised of the evaluation of their methods. Method developers with submissions that are classified as Category 2 or 3 are encouraged to provide additional information if available. A list of all the submitted methods and their classifications are posted for public review.

Usually, two ERP members (sometimes more) are assigned to lead the review of each Category 1 method. An ERP meeting is convened to review the methods. ERP meetings are open to all interested parties, and are usually well-attended events with about 50–60 attendees common. Each Category 1 method is reviewed and discussed by the ERP. If stakeholders have designated the method to be a dispute resolution method (as stated in the SMPR), then the ERP is asked to identify the single best candidate method to be adopted as a First Action *Official Method*. If the SMPR does not specify the need for a dispute resolution method, then the ERP may choose to adopt all methods that meet the SMPRs, or may choose to adopt the single best method in their collective, expert opinion.

In addition, an ERP may choose to require changes to a candidate method as part of its First Action adoption and/or identify issues that are required to be resolved prior to adoption as a Final Action *Official Method.*

Methods adopted by an ERP as First Action *Official Methods* may not be in AOAC *Official Methods* format. Method developers/authors are asked to assist AOAC to rewrite the method and accompanying manuscript into an AOAC-acceptable format.

Two-Year First Action Evaluation Period

Under the new pathway, a method may be designated as a First Action *Official Method* based on the collective judgment of an ERP. *Official Methods* remain as First Action for a period of about 2 years. During the First Action period, the method will be used in laboratories, and method users will be asked to provide feedback on the performance of the method.

As previously described, two (or more) ERP members are assigned to lead the review of candidate methods for adoption as First Action *Official Methods*. After a method has been adopted as First Action, these lead reviewers are expected to keep track of the use of and experience with the First Action *Official Method*. At the conclusion of the 2-year evaluation period, one or both of the lead reviewers will report back to the ERP on the experience of the First Action *Official Method.*

The presiding ERP will monitor the performance of the method, and, at the completion of the 2-year First Action evaluation period, determine whether the method should be recommended to the OMB for adoption as an AOAC Final Action *Official Method*.

It is also possible that First Action *Official Methods* are not recommended for Final Action. There are two possibilities for an ERP to decide not to proceed with a First Action method: (*1*) feedback from method users indicates that a First Action method is not performing as well in the field as was expected; or (*2*) another method with better performance characteristics has been developed and reviewed. In either case, the ERP may choose to repeal the First Action status of a method.

OMB Review

The OMB will review all methods recommended for Final Action or repeal by the ERP, and will consider a number of factors in their decision. A guidance document for factors to consider is provided on the AOAC website at http://www.aoac.org/vmeth/OMB_ERP_Guidance.pdf. Some of the factors identified by the guidance document for OMB consideration are (*1*) feedback from method users, (*2*) comparison to the appropriate SMPR, (*3*) results from single-laboratory validation, (*4*) reproducibility/uncertainty and probability of detection, (*5*) availability of reference materials, and (*6*) safety concerns.

Conclusion

The new pathway to *Official Methods*℠ is deliberately designed to avoid creation of elaborate review systems. The intent of the model is for method experts to use their scientific knowledge, experience, and good judgment to identify and adopt the best methods possible for the analytical need.

These methods are then published as First Action *Official Methods,* and used by analysts while additional information about the method is collected.

Method reviewers may consider other forms of information in lieu of the traditional collaborative study to demonstrate method reproducibility.

Additional Information

Coates, S. (2012) "Alternative Pathway," *Inside Laboratory Management* **16**(3), pp 10–12

Expert Review Panels, Policies and Procedures, AOAC INTERNATIONAL, http://www.aoac.org/News/EXPERT%20REVIEW%20PANELS%20final%20revision.pdf

Standard Format and Guidance for AOAC Standard Method Performance Requirement (SMPR) Documents, AOAC INTERNATIONAL, http://www.aoac.org/ISPAM/pdf/3.5%20SMPR%20Guideline%20v12.1.pdf

Guidance Documents

Requirements for First Action Official Methods℠ Status

See Figure 1 for process flowchart.

Expert Review Panels

(*1*) Supported by relevant stakeholders.

(*2*) Constituted solely for the ERP purpose, not for SMPR purposes or as an extension of an SMPR.

(*3*) Consist of a minimum of seven members representing a balance of key stakeholders. A quorum is the presence of seven members or 2/3 of total vetted ERP membership, whichever is greater.

(*4*) ERP constituency must be approved by the OMB.

(*5*) Hold transparent public meetings only.

(*6*) Remain in force as long as method in First Action status.

First Action Official Method℠ Status Decision

(*1*) Must be made by an ERP constituted or reinstated post March 28, 2011 for First Action *Official Method℠* status approval.

(*2*) Must be made by an ERP vetted for First Action *Official Method℠* status purposes by OMB post March 28, 2011.

(*3*) Method adopted by ERP must perform adequately against the SMPR set forth by the stakeholders.

(*4*) Method must be adopted by unanimous decision of ERP on first ballot. If not unanimous, negative votes must delineate scientific reasons.

(*5*) Negative voter(s) can be overridden by 2/3 of voting ERP members after due consideration.

(*6*) Method becomes Official First Action on date when ERP decision is made.

(*7*) Methods to be drafted into AOAC format by a knowledgeable AOAC staff member or designee in collaboration with the ERP and method author.

(*8*) Report of First Action *Official Method℠* status decision complete with ERP report regarding decision, including scientific background (references, etc.), to be published concurrently with method in traditional AOAC publication venues.

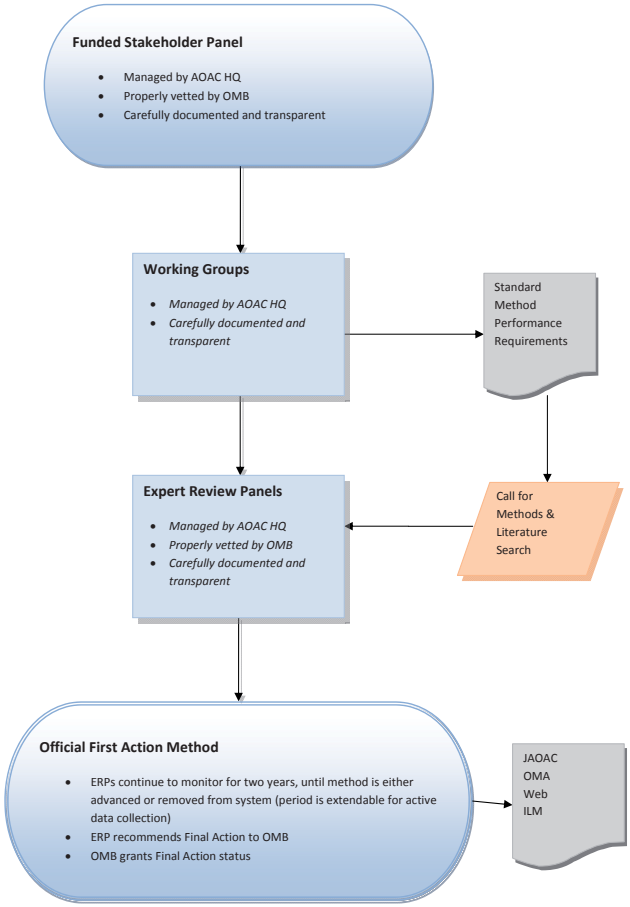


Figure 1. Summary of standards development through *Official Methods of Analysis*.

Method in First Action Status and Transitioning to Final Action Status

(*1*) Further data indicative of adequate method reproducibility (between laboratory) performance to be collected. Data may be collected via a collaborative study or by proficiency or other testing data of similar magnitude.

(*2*) Two years maximum transition time [additional year(s) if ERP determines a relevant collaborative study or proficiency or other data collection is in progress].

(*3*) Method removed from Official First Action and OMA if no evidence of method use available at the end of the transition time.

(*4*) Method removed from Official First Action and OMA if no data indicative of adequate method reproducibility is forthcoming as outlined above at the end of the transition time.

(*5*) ERP to recommend method to Final Action Official status to the OMB.

(*6*) OMB decision on First to Final Action status.

These guidance documents were approved by the AOAC Board of Directors on May 25, 2011. Revised in February 2014 to include the definition of a quorum under the section *Expert Review Panels*, item (*3*).

First Action to Final Action Methods: Guidance for AOAC Expert Review Panels

In December 2011, the Official Methods Board (OMB) approved a guidance document for ERPs to support their work as they deliberate on methods, adopt methods as Official First Action, and, subsequently, track method usage and performance between First Action status and Final Action consideration. The guideline is based on parameters of a method that the OMB will consider when deliberating on methods recommended for Final Action status. ERPs are to use this guideline in their deliberations.

ERPs working within the AOAC process may recommend a First Action status method be elevated to Final Action status. Such a recommendation leverages the ERP's high level of expertise supported by data from the initial evaluation, and results from the subsequent 2-year method performance evaluation period.

The OMB receives the recommendation with supporting documentation, and determines if Final Action status is warranted. OMB's review verifies the method process was conducted in compliance with the guidelines and protocols of the Association.

For transparency and to expedite the review process, the main areas OMB will review when evaluating ERP recommendations to promote methods to Final Action are listed below. Documentation of the areas listed below will also increase confidence in method performance and assist users to properly and safely perform the methods at their locations.

A. Method Applicability

(**a**) A method's applicability to the identified stakeholder needs is best assessed by the stakeholder panel and should be a part of the process from the onset. OMB liaisons will remind stakeholder panels to maintain this focus point.

(**b**) OMB may ask ERPs and stakeholder panels for feedback to improve the applicability of the method, such as potential method scope expansions and potential points of concern.

B. Safety Concerns

(**a**) A safety review must be performed for a method to be recognized as First Action.

(**b**) All safety concerns identified during the 2-year evaluation period must be addressed.

(**c**) Guidance and support can be obtained from the AOAC Safety Committee.

C. Reference Materials

(**a**) Document efforts undertaken to locate reference materials. Methods may still progress to Final Action even if reference materials are not available.

(**b**) Guidance and support can be obtained from the AOAC Technical Division on Reference Materials.

D. Single-Laboratory Validation

(**a**) Data demonstrating response linearity, accuracy, repeatability, LOD/LOQ, and matrix scope must be present. Experimental designs to collect this data may vary with the method protocol and the intended use of the method.

(**b**) Resources can be identified by the AOAC Statistics Committee.

E. Reproducibility/Uncertainty and Probability of Detection

(**a**) For quantitative methods, data demonstrating reproducibility and uncertainty must be present. Experimental designs to collect this data may vary with the method protocol, available laboratories, and the intended use of the method (i.e., collaborative studies, proficiency testing, etc.).

(**b**) For qualitative methods, data must be present demonstrating the probability of detection at specified concentration levels as defined by the SMPR. Experimental designs to collect this data may vary with the method protocol, available laboratories, and the intended use of the method.

(**c**) Guidance and support can be obtained from the AOAC Statistics Committee.

F. Comparison to SMPR

(**a**) Document method performance versus SMPR criteria. Note which SMPR criteria are met. For SMPR criteria not met, the ERP documents the reasoning why the method is still acceptable.

(**b**) Data is present to assure the matrix and analyte scopes are covered. This is critical for methods used for dispute resolutions.

G. Feedback from Users of Method

(**a**) Document positive and negative feedback from users of the method during the trial period.

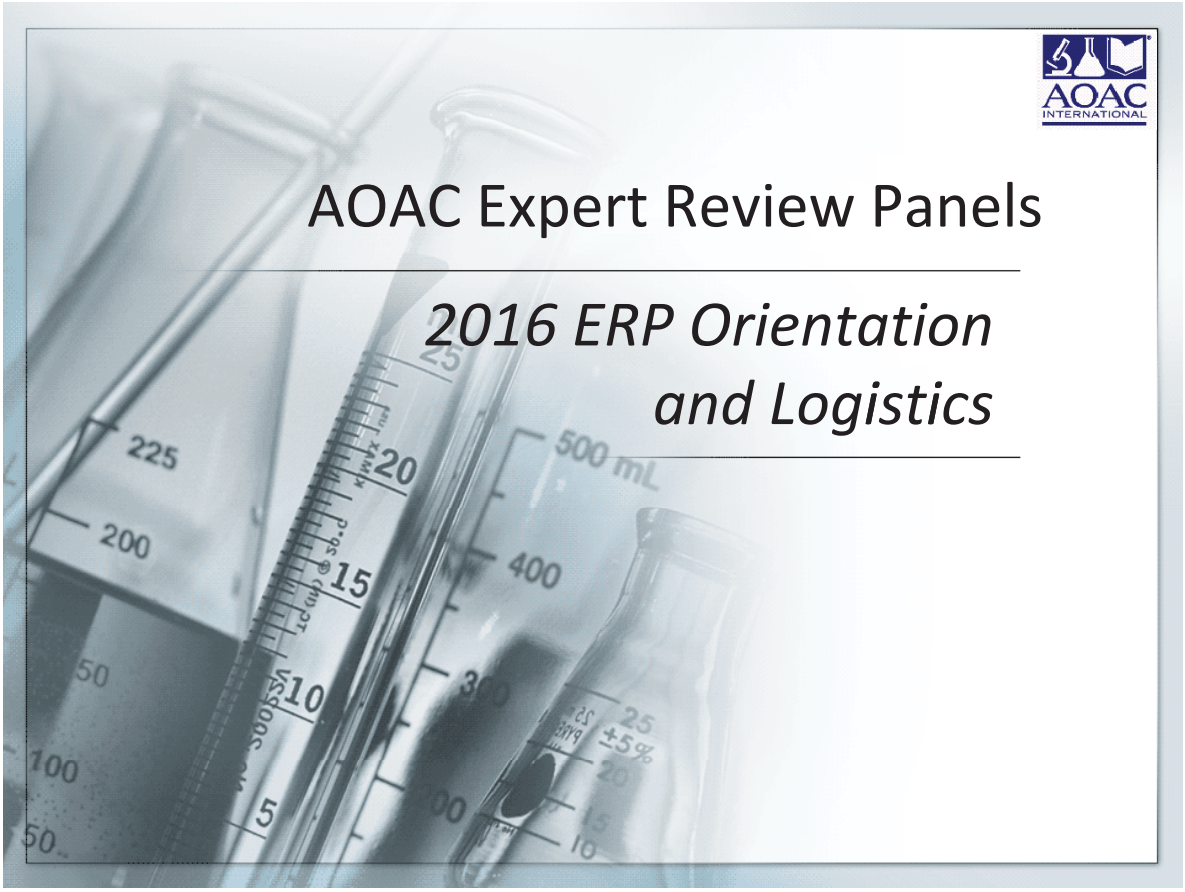
(**b**) Feedback from users demonstrating method ruggedness should be documented.

(**c**) Assess the future availability of vital equipment, reference materials, and supplies.

H. ERP Recommendations to Repeal First Action Methods

Recommendations to repeal First Action methods shall be accompanied with detailed reasons for the decision.

The First to Final Action guidance for ERPs was approved by the OMB in December 2011 and effective as of February 1, 2012.



AOAC Expert Review Panels

2016 ERP Orientation and Logistics

Session Syllabus

1. AOAC Method Submission
2. Recruitment of ERP Members
3. ERP Composition & Vetting Expertise
4. ERP Method Assignments
5. ERP Meeting
6. ERP Consensus
7. Post ERP Meeting
8. First Action to Final Action status
9. Method Modifications
10. Publications
11. Documentation
12. Summary of Responsibilities

TRACT 1

METHOD SUBMISSION

Paths to AOAC *Official Methods*

- AOAC Official Methods through AOAC Standards Development

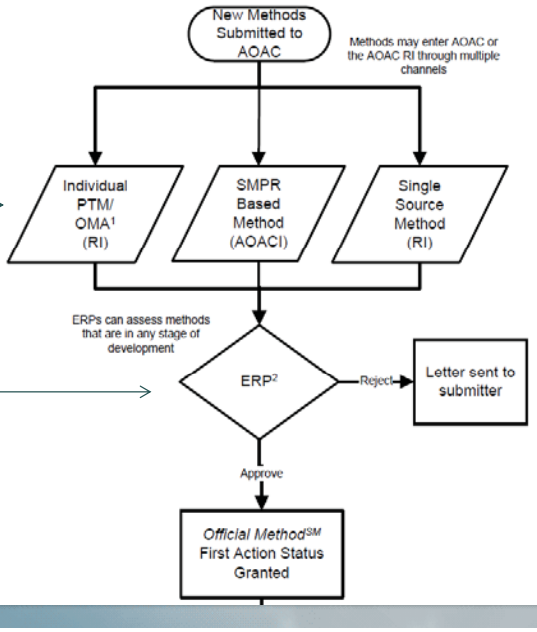
Road to First Action OMA Status

Terms:

- PTM – *Performance Tested Methods℠*
- RI – Research Institute
- ERP – Expert Review Panel
- OMB – Official Methods Board
- SP – Stakeholder Panel
- SMPR – Standard Method Performance Requirement

Three modes of entry and (program administration)

Expert Review Panels will review all methods for all three modes of entry.

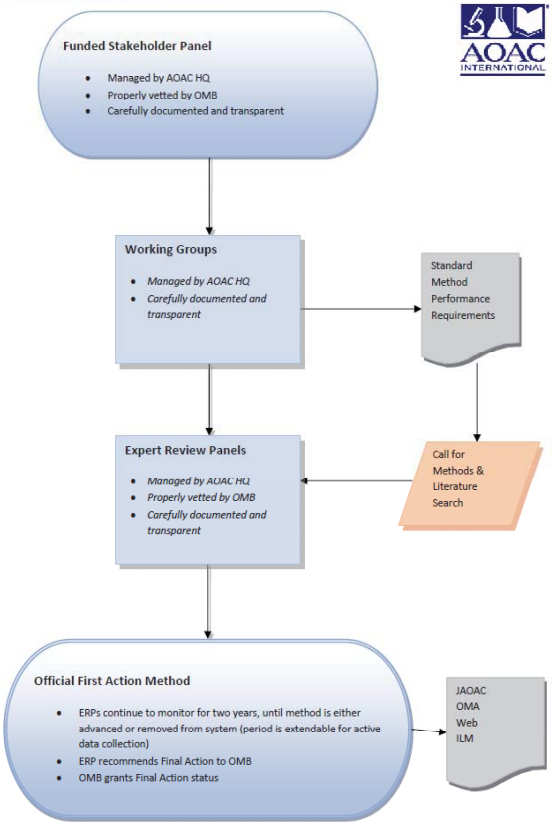


Note: Appeals process always available; see Alternative Pathway Guidelines for appeals process.

1 PTM certification previously issued, PTM reviewers will be ERP members
2 Unless otherwise provided for under a contractual agreement, AOAC will regularly convene ERPs twice a year: once during the Mid-Year Meeting and again during the Annual Meeting

Recap of the Overall Process for Methods Submitted in response to SMPRs or Call for Methods – aka "alternative pathway"

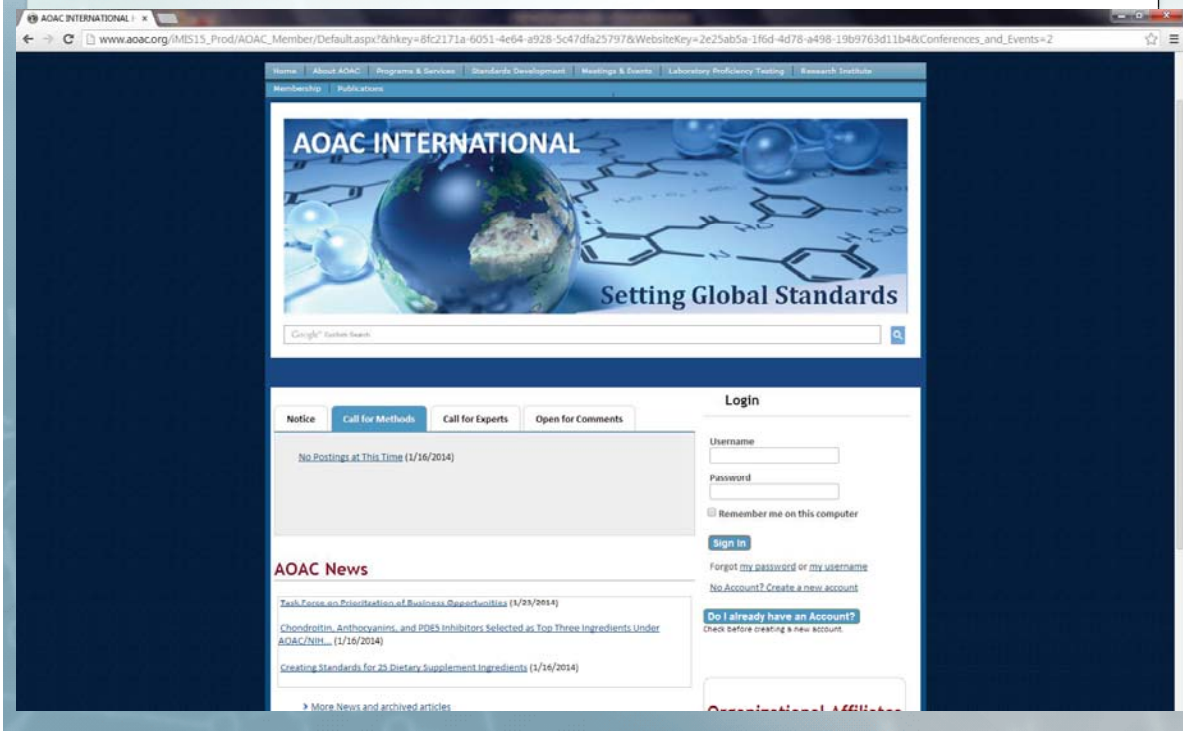
1. Allows AOAC to focus on projects addressing an urgent need of a critical mass of stakeholders.
2. Drives AOAC processes forward faster.
3. Assembles stakeholders (industry, government and academia) to neutral place to articulate and reach consensus on requirements and resolve conflicts.
4. Those requirements are codified and are published as "Standard Method Performance Requirements" (SMPRs).
5. Methods are solicited that purport to meet those requirements.
6. Expert review panels (ERPs) judge the methods against the SMPRs. Method(s) that best meet the SMPRs are adopted and designated "First Action" *Official Method of Analysis*.
7. Process for First Action status to Final Action status follows as the same process for all AOAC First Action *Official Methods*.



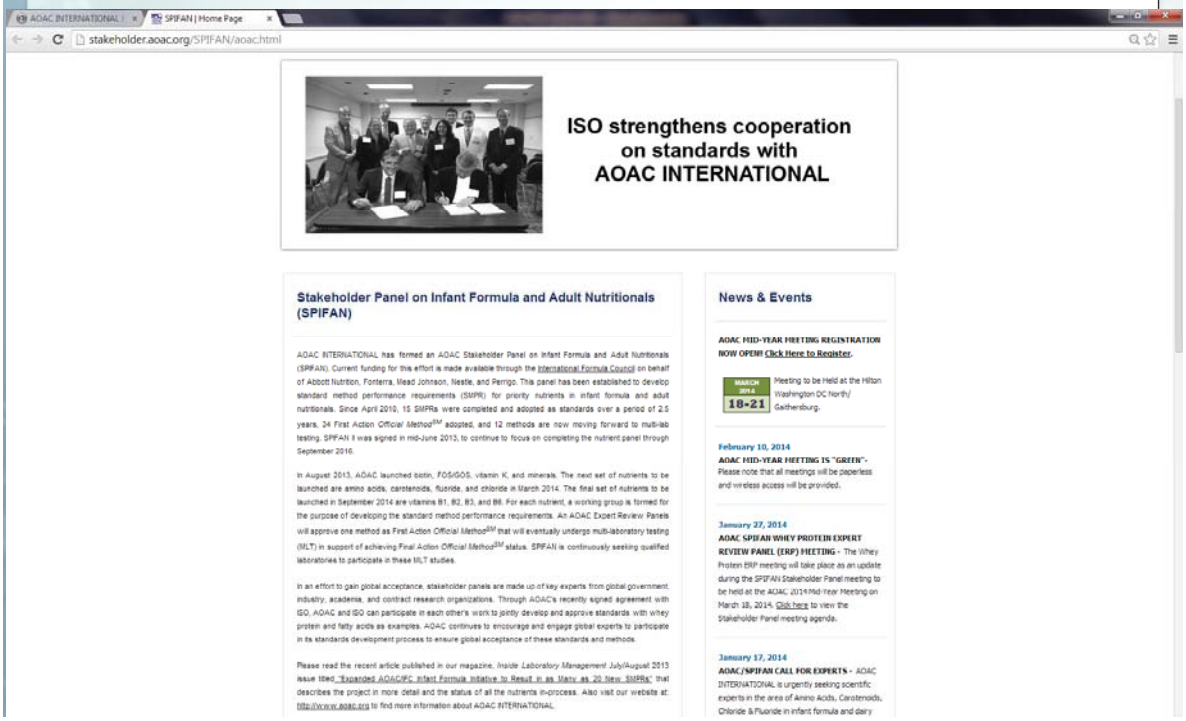
Method Submissions

- Method developers responding to an AOAC issued Call for Methods or to adopted standard method performance requirements (SMPRs) should submit their methods to AOAC INTERNATIONAL
- All other methods should be submitted to the AOAC Research Institute.
- Contact AOAC staff for details.

Calls for Methods



Call for Methods



December 19, 2013 AOAC/SPIFAN Community Update

STAKEHOLDER PANEL ON INFANT FORMULA & ADULT NUTRITIONALS (SPIFAN) NEWS

AOAC/SPIFAN CALL FOR CARNITINE METHODS EXTENDED

AOAC INTERNATIONAL invites method developers to submit Carnitine methods for consideration through the AOAC *Official Methods*℠ Program. Methods should meet or exceed the Standard Method Performance Requirement (SMPR). Click here to view Carnitine Call for Methods.

Interested method developers should provide a description and data demonstrating that the method will meet the SMPR. Click here to submit method(s). Deadline for submissions to be considered is **Friday, January 17, 2014**.

AOAC/SPIFAN CALL FOR EXPERTS

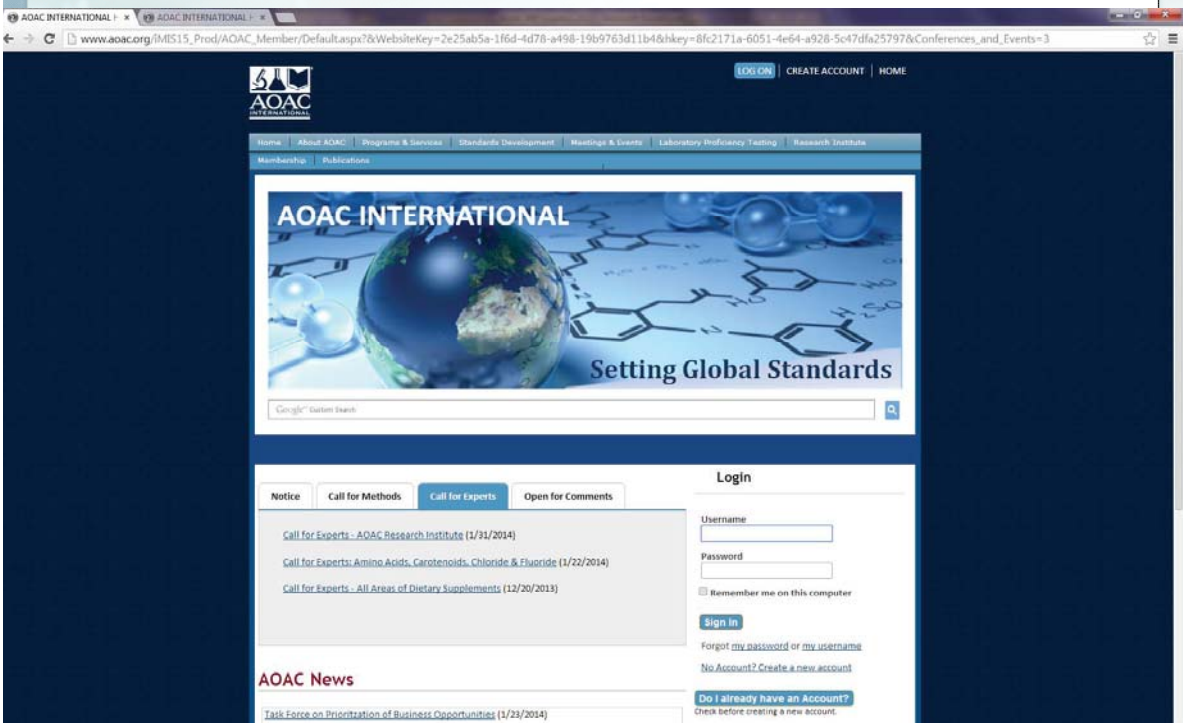
AOAC INTERNATIONAL is urgently seeking scientific experts in the area of Amino Acids, Carotenoids, Chloride & Fluoride in infant formula and dairy products to establish standard methods performance requirements (SMPRs). Click here to view Call for Experts.

SPIFAN ACTIVITIES AT AOAC INTERNATIONAL MID-YEAR MEETING (March 18-19, 2014)

TRACT 2

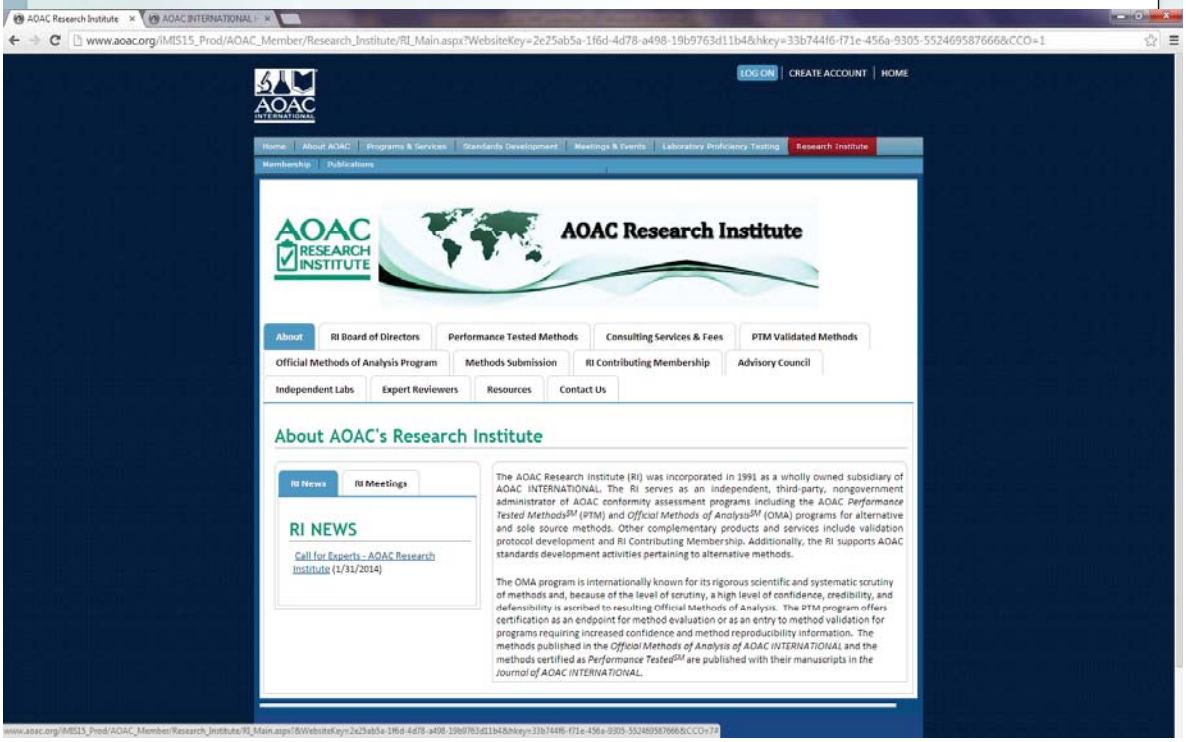
RECRUITMENT OF ERP MEMBERS

CALL FOR EXPERTS



CALL FOR EXPERTS

CALL FOR EXPERTS



Other Forms of Recruitment

- Official Methods Board
- Email Blasts to AOAC network
- Leveraging networks of Advisory Panel members, Working Group Members, AOAC Communities and Sections

REQUIREMENTS FOR ERP SERVICE

- Must have demonstrated expertise in the method, technology, analyte/matrix, etc… Be a subject matter expert.
- Must be able to attend ERP meetings
- Must be able to complete assigned reviews on time
- Must be prepared to speak on the method and share reviews during the meeting
- Must be proactive in tracking assigned First Action *Official Methods*
- Must be able to assist in peer reviewing paper for publication
- Must sign and submit AOAC Volunteer Acceptance Form

AOAC Policies

- AOAC INTERNATIONAL Antitrust Policy
- AOAC INTERNATIONAL Policy On The Use Of The Association Name, Initials, Identifying Insignia, Letterhead, And Business Cards
- AOAC INTERNATIONAL Policy And Procedures On Volunteer Conflict Of Interest
- Volunteer Acceptance Form

Antitrust Responsibilities

- AOAC activities frequently involve cooperative undertakings and meetings where competitors may be present, it is important to emphasize the ongoing commitment of our members and the Association to full compliance with national and other antitrust laws
- Association's structure is fashioned and its programs are carried out in conformance with antitrust standards.
- An equal responsibility for antitrust compliance - which includes avoidance of even an appearance of improper activity - belongs to the individual.
  - The appearance of improper activity must be avoided because actual proof of misconduct is not required only whether misconduct can be inferred from the individual's activities.
- Compliance with AOAC policy and guidelines involves not only avoidance of antitrust violations, but avoidance of any behavior which might be perceived as such.

Antitrust Policy Document

- The document states antitrust laws in general terms, and is not a summary of applicable laws.
- It is intended only to highlight and emphasize the principal antitrust standards which are relevant to AOAC programs and activities.
- Signing the AOAC INTERNATIONAL Volunteer Acceptance Form means that the signer has read, understand and agrees to comply with the policy.

USE OF THE ASSOCIATION NAME, INITIALS, IDENTIFYING INSIGNIA, LETTERHEAD, AND BUSINESS CARDS

- to protect the reputation, image, legal integrity and property of the Association.
- "The Board approves and encourages reference to the Association by name, either as AOAC INTERNATIONAL or as AOAC; or reference to our registered trademark, AOAC®, in appropriate settings to describe our programs, products, etc., in scientific literature and other instances so long as the reference is fair, accurate, complete and truthful and **does not indicate or imply unauthorized endorsement** of any kind.
- Neither the Association's name nor its insignia nor part of its insignia may be incorporated into any personal, company, organization, or any other stationery other than that of the Association;
- Please review instructions on use and sanctions for violations.
- Signing the AOAC INTERNATIONAL Volunteer Acceptance Form means that the signer has read, understand and agrees to comply with the policy.

Volunteer Conflict Of Interest

- It is the sense of AOAC that conflicts of interest or even the appearance of conflicts of interest on the part of AOAC volunteers should be avoided
- Where this is not possible or practical under the circumstances, there shall be written disclosure by the volunteers of actual or potential conflicts of interest in order to ensure the credibility and integrity of AOAC. Such written disclosure shall be made to any individual or group within the Association which is reviewing a recommendation which the volunteer had a part in formulating and in which the volunteer has a material interest causing an actual or potential conflict of interest.
- AOAC requires disclosure of actual or potential conflicts of interest as a condition of active participation in the business of the Association. The burden of disclosure of conflicts of interest or the appearance of conflicts of interest falls upon the volunteer.

Volunteer Conflict Of Interest Policy Document

- Contains illustrations of apparent or direct conflicts of interest, but not all inclusive
- Contains guidance on Dos and Don’ts for volunteers
- Signing the AOAC INTERNATIONAL Volunteer Acceptance Form means that the signer has read, understand and agrees to comply with the policy.

TRACT 3

ERP COMPOSITION & VETTING EXPERTISE

ERP Composition

- Call for Experts or Volunteers is issued.
- Members must be vetted by AOAC Official Methods Board (OMB).
  - Demonstrated expertise
  - Diversity and balance of the overall expert review panel
- AOAC volunteer appointment
  - Serve at the pleasure of the President of AOAC INTERNATIONAL
- Additional members may be added.
- Can have non-voting members
- OMB assigns an OMB member to serve as a representative on each ERP

ERP SELECTION PROCESS

- AOAC paid consultants and AOAC staff should not act as Chairs of ERPs.
- Members of the BoD may act as voting members but it is recommended that they sit as non-voting members of the panel, unless the CSO can demonstrate that there are so few experts in the field available to the community that they are needed to move the project forward.
- Paid consultants of AOAC and AOAC staff may not serve as voting members on ERPs.
- If a single business location is represented by more than one person on an ERP, that location shall have only one vote.
- The Chair of the ERP must be a member of AOAC INTERNATIONAL.

Vetting Process

AOAC Chief Science Officer

- Reviews all candidates and supporting documentation for expertise
- Makes a recommendation for an ERP slate

Official Methods Board

- Reviews proposed recommended ERP slate
  - Expertise
  - Balance of panel
  - Conflicts of interest
- Renders decision on proposed ERP members and a Roster is formed.

TRACT 4

ERP METHOD ASSIGNMENTS

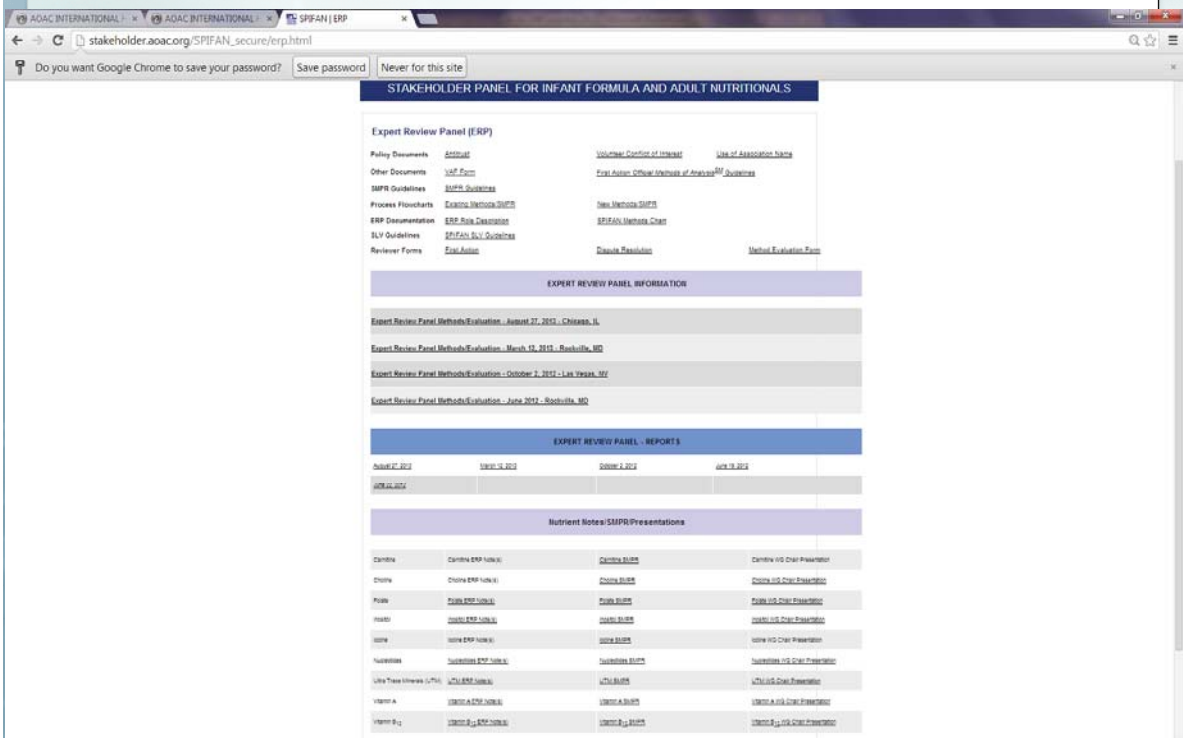
ERP Method Assignments

- A primary and secondary reviewer is assigned to every method.
  - In depth review via review form
  - Prepare to attend and speak on the method and make a recommendation for ERP discussion and consideration.
  - Review forms are completed and returned to AOAC staff in advance of the meeting.
- Members of both Committee on Safety and Committee on Statistics serve as advisory resources for all ERPs

ERP REVIEWS

- Primary and Secondary Reviewers and/or entire ERP conduct in-depth review of method and any supporting information.
  - In-depth review is done electronically through password protected website access and is completed prior to the in-person meeting.
  - Deadlines for submission of reviews
  - Depending on the number of methods 15 to 30 days for review
  - Track and present feedback on assigned First Action *Official Methods*.
  - Present on the method during the meeting and can make the motion to adopt the method.
  - Can recommend additional feedback or information for Final Action consideration

ERP REVIEWS



AOAC INTERNATIONAL

ERP REVIEWS

- **In your judgment, does the method sufficiently meet the Standard Method Performance Requirements (SMPR)?**

- In your judgment, is the method scientifically sound and can be followed?
- In your judgment, what are the strengths and weaknesses of the method?
- In your judgment, how do the weaknesses weigh in your recommendation for the method?
- In your judgment, will the method serve well the stakeholder community that will use the method?
- In your judgment, what additional information may be needed to further support the method meeting the SMPR?

TRACT 5

ERP MEETINGS

ERP Meetings

- ERPs will meet in person at a minimum of twice a year and up to four times per year:
  - AOAC Mid-Year meeting (DC metro area)
  - AOAC Annual Meeting.
- At the ERP meeting:
  - **Primary and secondary reviewers or entire ERP** will present their reviews and makes a motion/recommendation to the ERP whether or not to adopt the method as First Action OMA.
  - ERP discusses the method.
  - ERP renders a decision on First Action status.
  - ERP renders decisions on modifications to First Action methods only.
- If the method is adopted
  - ERP decides on what additional information is needed to recommend the method for Final Action status

ERP MEETINGS

- MEETINGS ARE HELD IN-PERSON, HOSTED BY AOAC
- A QUORUM IS THE PRESENCE OF SEVEN (7) MEMBERS OR 2/3 OF THE TOTAL VETTED ERP, WHICHEVER IS GREATER.

IF NO QUORUM, THEN NO MEETING!

ERP MEETINGS

- REVIEWERS PRESENT THEIR REVIEWS AND MAY INITIATE A MOTION TO ADOPT THE METHOD IF THEY CHOOSE
  - Chair recognizes the reviewers
  - Primary and secondary / ERP reviews are presented.
    - If in favor, they may make and second a motion to adopt or not adopt the method
    - Chair can then entertain discussion on the method
    - Chair can call for a vote once deliberation is complete

ERP MEETING - Discussions

- In your collective judgment, is the method scientifically sound and can be followed as written?
- **In your collective judgment, does the method sufficiently meet the Standard Method Performance Requirements (SMPR)?**
- In your collective judgment, what are the strengths and weaknesses of the method?
- In your collective judgment, do the weaknesses outweigh the strengths in your recommendation for the method?
- In your collective judgment, is the method safe and can it serve well the stakeholder community that will use the it?
- In your collective judgment, is additional information needed to before considering this method for First Action OMA status?

TRACT 6

ERP CONSENSUS

ERP CONSENSUS

- First Action Official Methods status is granted:
- Method must be adopted by unanimous decision of ERP on first ballot, if not unanimous, negative votes must delineate scientific reasons.
- Negative voter(s) can be overridden by 2/3 of voting ERP members after due consideration.
- Method becomes First Action on the date when ERP decision is made.

ERP CONSENSUS

- The ERP may then reach consensus on any additional information that it needs to review to be able to make a recommendation for Final Action *Official Methods* status.
- This is a separate motion.

TRACT 7

POST ERP MEETING

Post ERP Meeting

- An ERP report with the decisions of the ERP will be drafted
  - Review and approval by ERP chair
  - Posted on website within 15 business days after the ERP meeting
- AOAC staff will send notification to method authors/submitters regarding outcomes on specific methods

TRACT 8

FIRST ACTION TO FINAL ACTION STATUS

ERP Tracking

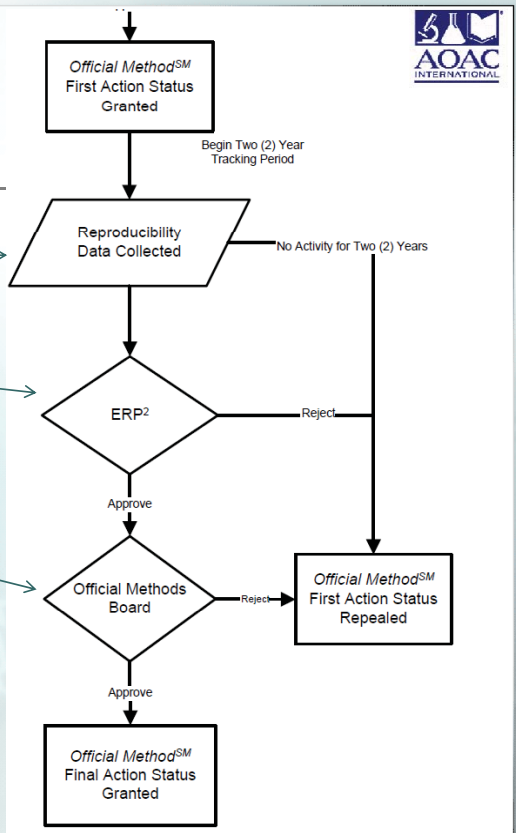
- Between First Action and Final Action:
  - The primary and secondary reviewers track the methods on behalf of the ERP over this time period.
    - Based on information from method authors, laboratories using the method, general community feedback, additional laboratory work
    - Are ERP recommendations being fulfilled?
    - Is the method meeting the standard criteria more closely?
    - How well is community guidance and OMB guidance being reflected?
  - Updates on the method are given by the primary and secondary reviewers during the ERP meetings.
  - At the end of two years, ERP makes a recommendation to OMB for Final Action status, repeal, or continuance.

Road to Final Action OMA Status

Method reproducibility must be demonstrated before Final Action consideration.

ERP determines if sufficient evidence merits a recommendation for Final Action status or repeal.

- Only the OMB promotes a method to "Final Action" status or repeal the method.
- Methods that did not meet the bar would be repealed.
- Same for all method submissions



Terms:

- PTM – *Performance Tested Methods℠*
- RI – Research Institute
- ERP – Expert Review Panel
- OMB – Official Methods Board
- SP – Stakeholder Panel
- SMPR – Standard Method Performance Requirement

Note: Appeals process always available; see Alternative Pathway Guidelines for appeals process.

1 PTM certification previously issued, PTM reviewers will be ERP members
2 Unless otherwise provided for under a contractual agreement, AOAC will regularly convene ERPs twice a year: once during the Mid-Year Meeting and again during the Annual Meeting

Path to Final Action

Review of ERP Method Recommendations

What to Expect from AOAC Official Method Board (OMB)

Standard Method Performance Pathway

1. Standard Method Performance Requirements authored by Working Groups and established by Stakeholders
2. Expert Review Panel (ERP) vetted by OMB
3. ERP approves methods for First Action
4. Method reproducibility data collected
5. ERP monitors method performance
6. ERP recommendations sent to OMB within 2 years
   - Final Action, First Action continuation, or Repeal

OMB Liaison

- OMB member or designee is assigned to your ERP
- Liaison monitors First Action to Final Action process
- Monitors ERP's documentation of all items in OMB Guidance document (OMA Appendix G)

Method Applicability

- Determine how method meets stakeholder's needs
  - scope, accuracy, precision, etc.
- Are ERP recommendations & improvements implemented?
- Assess method limitations & concerns

Safety Concerns

- Safety review completed for First Action
  - Participation by Safety Committee
- All safety issues identified during 2 year review addressed
  - Participation by Safety Committee

Reference Materials

- Identification of potential reference materials (RM)
  - If none found, define alternative options
- RM performance expectations

Available resource is the AOAC Technical Division on Reference Materials (TDRM)

Single Laboratory Validation

Chemistry

- Linearity
- Accuracy
- Repeatability
- LOD / LOQ
- Matrix scope
- Selectivity

Microbiology

- Inclusivity/Exclusivity
- Robustness
- Repeatability
- POD or equivalent
- Matrix scope

AOAC Committee on Statistics is your resource

Quantitative Reproducibility/Uncertainty

- Experimental designs may vary
  - Collaborative study
  - Proficiency Testing data
  - Multi-lab study variations
- Committee on Statistics
  - is available to discuss new study design protocols
  - Formalized tools were presented at the 2013 Annual Meeting

Qualitative Reproducibility/Uncertainty

- Experimental designs may vary
- Committee on Statistics is available to discuss new study protocols designs

Compare to SMPR

- Method meets Performance Criteria
- Method does not meet Performance Criteria
  - Acceptable or not? List reasoning
- Document acceptability to Stakeholders

Feedback from Users

- Solicit and document user feedback
  - ERP Chair determines mechanism
  - May take form of
    - Proactive calls to users
    - Tally of incoming calls
    - Emails
    - Web surveys

Feedback from Users

- Method performance
- Safety Concerns
  - Warnings
  - Alternatives
- Equipment and supply availability
  - Readily available
  - Practicality
  - Suggested improvements
  - Failures
- Reference material availability

September 20, 2004

ERP SUMMARY FOR FIRST TO FINAL ACTION METHOD RECOMMENDATION

AOAC No.	NAME OF METHOD

GUIDANCE FOR AOAC ERPS - APPENDIX G[1]	**Considered?**	**Comments/Reference if applicable**
Method Applicability		
ERP First Action to Final Action recommendations & improvements		
Draft Final Action method reviewed by ERP		
Safety Concerns		
Reference Materials		
Single Laboratory Validation		
Reproducibility/Uncertainty and Probability of Detection		
Comparison to SMPR (SMPR criteria met?)		
Feedback from Users of Method		

DOCUMENTATION	**Available?**	**Comments**
Safety Evaluation		
Reference Materials		
SLV or PTM		
Approved Validation Protocols		
Statistics Review		
Method Published in OMA		
Method Performance vs SMPR criteria		
Feedback Information		
Additional Recognition(s)		
ERP Reports		
Manuscript(s) Published in JAOAC		
ERP Method Recommendation (Final Action/Repeal/Continuation)		

[1] *Official Methods of Analysis of AOAC INTERNATIONAL*, Appendix G: Procedures and Guidelines for the Use of AOAC Voluntary Consensus Standards to Evaluate Characteristics of a Method of Analysis, p.3 *"First Action to Final Action Methods: Guidance for AOAC Expert Review Panels."*

ERP SUMMARY FOR FIRST TO FINAL ACTION METHOD RECOMMENDATION

AOAC 2012.25	**Residues of Three Triphenylmethane Dyes and Their Metabolites (Malachite Green, Leuco Malachite Green, Crystal Violet, and Brilliant Green) in Aquaculture Products** **Liquid Chromatography/Tandem Mass Spectrometry**

GUIDANCE FOR AOAC ERPS - APPENDIX G[1]	**Considered?**	**Comments/Reference if applicable**
Method Applicability	Yes	Triphenylmethane dyes as specified in applicability statement.
ERP First to Final Action recommendations & improvements implemented/addressed	Yes	
Draft Final Action method reviewed by ERP	Yes	
Safety Concerns	Yes	Completed and discussed during ERP meeting
Reference Materials	Yes	Currently no reference materials available for these types of drugs
Single Laboratory Validation	Yes	Hurtaud-Pessel et al., *J. AOAC Int.* **96**, 1152(2013) Andersen et al., *J. AOAC Int.* **98**, 636(2015) – modification – matrix extension
Reproducibility/Uncertainty and Probability of Detection	Yes	Schneider & Andersen *J. AOAC Int.* **98**, 658(2015)
Comparison to SMPR (SMPR criteria met?)	Yes	SMPR 2009.001 – SMPR for Quantitative Methods for Drug Residues in Shrimp, Tilapia, Catfish, and Salmon; SMPR criteria met according to ERP
Feedback from Users of Method	Yes	Discussed in ERP Meeting

DOCUMENTATION	**Available?**	**Comments**
Safety Evaluation	Yes	Completed; Discussed in ERP meeting
Reference Materials	No	None specified in SMPR; none available
SLV or PTMs	Yes	Hurtaud-Pessel et al., *J. AOAC Int.* **96**, 1152(2013) Andersen et al., *J. AOAC Int.* **98**, 636(2015)
Approved Validation Protocols	No	Used SMPR; OMA appendix D, and help from Chemical Contaminants Community subgroup
Statistics Review	Yes	Completed
Method Published in OMA	Yes	2012.25
Method Performance vs SMPR criteria	Yes	SMPR 2009.001 – SMPR for Quantitative Methods for Drug Residues in Shrimp, Tilapia, Catfish, and Salmon
Feedback Information	Yes	Discussed in ERP meeting
Additional Recognition(s)	No	
ERP Reports	Yes	10/2012; 12/2015
Manuscript(s) Published in JAOAC	Yes	Hurtaud-Pessel et al., *J. AOAC Int.* **96**, 1152(2013) Andersen et al., *J. AOAC Int.* **98**, 636(2015) Schneider & Andersen *J. AOAC Int.* **98**, 658(2015)

ERP Method Recommendation (Final Action/Repeal/Continuation)	**Final Action**	**Method scope expanded and the latest version of the method approved by ERP is in Collaborative Study Manuscript published in 2015 by Schneider and Andersen.**

ERP Recommendations

- Supply all documentation to AOAC by established deadline
  - Documentation includes ERP review details
- Representative from ERP present at OMB review meeting
- If method to be repealed, document reasoning

TRACT 9

PUBLICATIONS

Publication of First Action Methods

- Any approved method(s) along with supporting manuscript(s) and documentation sent to AOAC Publications after the meeting.
  - AOAC Official Methods number assigned.
  - Method and method manuscript prepared for publication in the *Official Methods of Analysis of AOAC INTERNATIONAL* and in Journal of AOAC INTERNATIONAL
  - Updates on methods approved or status changes are published in the Inside Laboratory Management magazine and on the AOAC website

Format for AOAC *Official Methods of Analysis*

The language of the method should be concise and completely free from ambiguity. Conciseness is desirable, both to ensure clarity and to save space. Whenever there is a conflict between clarity and style, clarity is more important.

Present Tense and Imperative Mode
- Check sentences that do not begin with a verb and change them, if feasible, to the imperative mode (e.g. Pipet 10 mL..., Stir..., etc.). Exceptions are: use of adverb modifier ("Accurately weigh..."), prepositional clause ("For refined sugars, use..."), permissive statements ("Ferric hydroxide may be used..."), and statements in the "Principle" section.

Abbreviations
- Most abbreviations are the same as those used by Chemical Abstracts. Do not use abbreviations in titles and headings. See the *Definitions of Terms and Explanatory Notes*.

Repetition and Redundancy
- Eliminate repetition and redundancy as far as possible; use only for emphasis. Do not use "distilled" with water, "concentrated" with common acids, "95%" with alcohol, or "ACS" with reagents covered by ACS specifications. These are understood by definition.

Terminology, Formulae and Chemical Names
- For names of chemical compounds, use the spelling, hyphenation, and word division given in Chemical Abstracts. Use a national pharmacopeia for names for drugs. Use ISO nomenclature for pesticides and Codex nomenclature for names of food additives and color additives.

Consistency
- Watch for internal contradictions in the text: volumes that do not add up or that exceed the capacity of the container; too abrupt a transition from one operation to another (a line may be omitted); and impractical or impossible numbers (e.g., 100 g NaCl will not dissolve in 100 mL water).

Cross-references
- All new AOAC methods should be written as complete and self-contained as practical. Do not refer to other AOAC methods. If part of a procedure in an *Official Method*℠ is taken from material previously published elsewhere, incorporate those steps in the method rather than referring the analyst to another publication.

Definitions
- The section "Definition of Terms and Explanatory Notes," *Official Methods of Analysis of AOAC INTERNATIONAL*, is the basic guide to conventions and consistency.

Illustrations and Tables
- If symbols are used on the figure, include an explanation in the caption or text. Provide descriptive titles for tables. Explain any obscure headings in a footnote.

Bibliographic References
- Check all references for accuracy. Use standard Chemical Abstracts abbreviations for *Journal* titles. In general avoid references in method. Cite background references in the "Introduction" or "Discussion" section of the collaborative study manuscript -- not in the method. If part of a procedure in an *Official Method*℠ is taken from material previously published elsewhere, incorporate those steps in the method rather than referring the analyst to another publication.

Safety
- All methods must be reviewed for safety and potential hazards. Methods should automatically incorporate cross-references to the safety statement(s), or present questioned conditions to the attention of the Committee on Safety for resolution.
- Decisions regarding inclusion of safety statements should be practical, recognizing that overuse will be self-defeating.
- Methods that create toxic, obnoxious or environmentally hazardous fumes and wastes should contain practical directions for disposal.

Checking Edited Copy and Proofreading
- The author must review a copy of the original version and edited copy to ensure that there has been no change in meaning, to correct typographical errors, and to answer any questions posed by the editor. The author must review the typeset method for accuracy.

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Online Technical Resources

Method Development, Optimization & Validation
- OMA - Appendix F - Guidelines for Standard Method Performance Requirements
- Homogeneity
- Guide for Writing Methods in AOAC Format
- Statistics Protocol Review Form
- OMA - Appendix D: Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis
- OMA - Appendix G: Procedures and Guidelines for the Use of AOAC Voluntary Consensus Standards to Evaluate Characteristics of a Method of Analysis
- OMA - Appendix I: AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Biological Threat Agent Methods and/or Procedures
- OMA - Appendix J: AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Microbiological Methods for Food and Environmental Surfaces
- OMA - Appendix K: Guidelines for Dietary Supplements and Botanicals
- OMA - Appendix L: AOAC Recommended Guidelines for Stakeholder Panel on Infant Formula and Adult Nutritionals (SPIFAN) Single-Laboratory Validation
- OMA - Appendix M - Validation Procedures for Quantitative Food Allergen ELISA Methods: Community Guidance and Best Practices
- Safety Checklist

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- OMA - Appendix A: Standard Solutions and Reference Materials
- OMA - Appendix D: Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis
- OMA - Appendix H: Probability of Detection (POD) as a Statistical Model for the Validation of Qualitative Methods

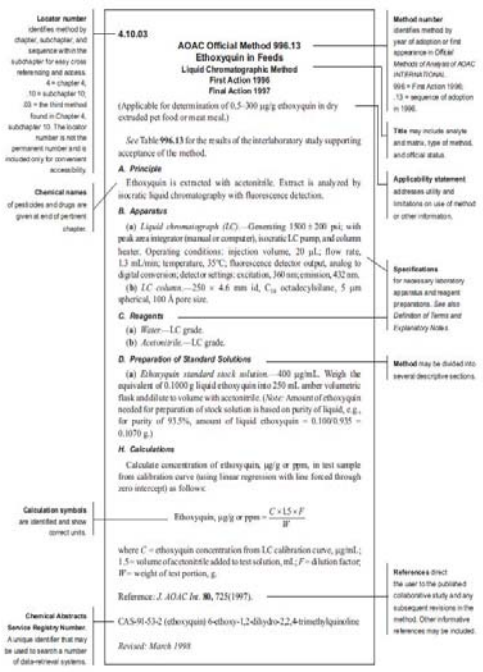
Miscellaneous
- Definition of Terms and Explanatory Notes
- OMA - Appendix B: Laboratory Safety
- OMA - Appendix E: Laboratory Quality Assurance
- OMA - Appendix C: Reference Tables

All resources are accessible at
http://www.aoac.org/imethguidelines.htm

For questions, please contact:
P 301-924-7077 x157 E dmckenzie@aoac.org

Guide to Method Format

(Method shown is incomplete to allow space for description.)



The AOAC style used for preparing methods for publication in the *Official Methods of Analysis of AOAC INTERNATIONAL* includes the following essentials:

- ✓ Standardized format that follows the order of laboratory operations.
- ✓ Use of the imperative mode.
- ✓ Cross-references to identical reagents, apparatus, and operations.
- ✓ Use of standardized definitions, terminology, and style.
- ✓ Use of accepted abbreviations and simplifications.
- ✓ Use of SI units
- ✓ Methods should be written as complete and self-contained as practical.
- ✓ Normality should be referred in terms of Molarity.
- ✓ ppm should be changed to mg/kg or mg/L
- ✓ ppb should be changed to ng/g or ng/mL
- ✓ ppt should be changed to pg/g or pg/mL

FORMAT OF AOAC® *OFFICIAL METHODS of ANALYSIS OF AOAC INTERNATIONAL*

Title:
- Includes analyte being determined, type of matrix (matrices), and analytical technique used for analysis.

Applicability:
- Includes list of matrix(es) along with specific matrix types and range or limits of determination or detection.

Precautions:
- Makes an analyst aware of hazardous materials used in analysis.

Data Collection:
- Table(s) that presents performance parameters including matrices tested in a collaborative study, levels of analyte(s), % recovery, RSD_r, RSD_R, s_r, s_R, HORRAT, number of observations, etc

Principle:
- Explains scientific premise on which the method is operates specifically the mechanism of the analysis.

Apparatus:
- Lists the equipment that requires assembly or that has specifications critical to the method performance. Describe equipment in terms of performance characteristics.

Reagents:
- List the reagents with amounts and appropriate units needed to conduct the analysis and describe the reagents in terms of performance characteristics.

Sample and Test Portion Preparation:
- Describe the preparation of samples and the test portion.

Determination:
- Describes the actual analysis.

Calculations:
- Section that explains how to calculate final results; presented in a form of equation or description.

Other sections as needed

REFERENCING *AOAC® OFFICIAL METHODS*℠

When referencing *AOAC® Official Methods*℠, only the method number should be used as seen in the following example:

(1) *Official Methods of Analysis of AOAC INTERNATIONAL* (2012) 19th Ed., AOAC INTERNATIONAL, Gaithersburg, MD, USA, Official Method **2008.01**

Revised October 2013

Publication of First Action Methods

NO OMA NUMBER ASSIGNED

UNTIL ALL DOCUMENTATION SUBMITTED

1. Method incorporating ERP revisions (preferably in AOAC Format)
2. Method Manuscript incorporating ERP revisions (in AOAC Format)
3. Signed AOAC Copyright Authorization form

Format for AOAC First Action *Official Methods* Manuscripts and Protocols

FORMAT FOR FIRST ACTION OMA MANUSCRIPTS

TITLE: Title of manuscript includes method title which includes the analyte(s), matrix(es), and analytical technique, if applicable. It may also include a *common* method name and ends with "Collaborative Study."

AUTHOR(S): Provides authors' full (e.g. no initials) names and contact information.

ABSTRACT:
- ✓ Specific information on the method and study.

INTRODUCTION:
- ✓ Information on why collaborative study was conducted, how many collaborators participated in the study, previous work done, and information on compound or process that was studied.

COLLABORATIVE STUDY:
- ✓ Information on matrices and number of test samples tested, test sample preparations, instructions for collaborators, etc.

METHOD:
- ✓ Written in AOAC style.

COLLABORATORS' COMMENTS:
- ✓ Any comments and suggestions received from collaborators and information on how they were addressed, e.g., incorporating instructions into the method, etc.

RESULTS AND DISCUSSION:
- ✓ Information on type of statistical analyses performed on raw data, reasons for rejecting some of the data, discussion of results with references to tables and figures, discussion of the method performance, etc.

RECOMMENDATION:
- ✓ Recommendation to adopt method First Action.

ACKNOWLEDGMENTS:
- ✓ Full names and addresses of all collaborators that participated in the study.

REFERENCES:
- ✓ Included all references cited in the text.

APPENDICES or **FIGURES AND TABLES:**
- ✓ Include any figures and tables that may make the manuscript and the performance of the method easier to understand and interpret.

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- OMA - Appendix C: Reference Tables

All resources are accessible at
http://www.aoac.org/vmethodguidelines.htm

For questions, please contact:
P 301-924-7077 x157 E dmckenzie@aoac.org

TRACT 10

MODIFICATIONS

Modifications of Methods

- During First Action and Final Action, methods can be modified or extended to additional matrixes and/or analytes.

Submitting a Modification

Standards Development

- Contact staff and they will let you know the best way to submit the modification information and any additional requirements.
  - Staff will inform of the appropriate mechanism to submit a modification.
- Fully revised method manuscript and a revised version of the AOAC OMA method, both in OMA format, must be submitted.

Research Institute

- Submit request for modifying a method through the AOAC website.
  - AOAC > Research Institute > Method Submission
  - AOAC RI Application for Method Change or Modification
- Fully revised method manuscript and revised method, both in OMA format, must be submitted.

Processing Modifications

ERPs from Standard Development and Research Institute

- Review of the modification will undergo a preliminary review by at least the AOAC CSO.
  - Comments to be shared with method author.
- Original ERP reviewers will be assigned to review the method
- Method will be added to ERP agenda for their next meeting

Approval of Modifications

- If ERP approves a method modification including extensions, then the method begins a new two (2) year period.

- If the method modification is to correct an editorial error, then the method, then there is no change.

Method modifications require substantiation of the modification or extension with proof of method performance as deemed suitable by the EPR.

TRACT 11

DOCUMENTATION

Reports and Documentation

- AOAC staff or designee will capture the decisions and action items into an ERP report.
- The draft report will be sent back to the ERP Chair whose responsibility it is to sign off on the report once approved.
- The report is then distributed to the ERP.
- ERP is responsible for a drafting a written recommendation to the OMB for each method at a maximum of two years following adoption as First Action OMA
- Approved methods from the ERP meetings are published in the OMA and in the *Journal of AOAC INTERNATIONAL*.
- Meeting overviews are published in the AOAC *Inside Laboratory Management* magazine.

TRACT 12

SUMMARY OF RESPONSIBILITIES

Roles and Responsibilities

- Expert Review Panel:
  - Review methods and meet in person to discuss and render decisions on methods for First Action *Official Methods* status.
  - Track First Action *Official Methods*
  - Modify First Action methods if necessary
  - Make recommendations on First Action methods no more than 2 years after adoption to OMB.
- Official Methods Board:
  - Vet and approve ERP membership
  - Assign OMB liaison to be a resource to the ERP
  - Review ERP recommendations and render decisions (*Final Action, Repeal or remain First Action*) on First Action OMAs
- AOAC Staff
  - Coordinate the ERP and meetings, facilitate reviews, document ERP actions/decisions.
  - Issue necessary calls for experts and methods

Task Force on Communication/ ERP Best Practices

Recommendations for Staff

- Regularly debrief with ERP Chairs for input after meetings
- ERP background and training materials on website
- Offer orientation on a regular basis, to all ERP chairs and potential members, wider distribution of training materials
- Execute post training surveys
- Clearly outline expectations of reviewers prior to meeting: attendance is mandatory, cursory review of all methods to be discussed
- Encourage all method authors to attend ERP: helps process move smoothly and authors will only be privy to full discussion if they attend
- Establish a codification system in OMA for “dispute resolution methods” *
- Investigate ways to elevate the level of prestige for participation in an ERP.

** Project specific*

Task Force on Communication/ ERP Best Practices

Best Practices for ERP Chairs

1. Work closely with staff during the orientation period for ERP
2. Clearly understand consensus and quorum rules
3. Discourage abstentions unless a true conflict of interest is present; *use discretion as necessary when determining if a vote allows a method move forward.*
4. Encourage ERP reviewers to be fully prepared
5. Add brief orientation to ERP meeting agenda
6. Where in a stakeholder panel community requires only one method is desired, a 2 step process that considers multiple methods may be adopted as First Action and assessment of the best method is determined during follow up ERP meetings.
7. When considering methods for repeal, advise ERP members that repeal does not discredit method, it is simply a procedural determination that a method will not be moved forward.

Expert Review Panels

The ERPs review and approve appropriate methods (as submitted or modified) for adoption as First Action Official Methods or for further validation. ERPs also make recommendations regarding Final Action Official Methods status.

Expert Review Panels

- Must be supported by relevant stakeholders.
- Constituted for the review of methods, not for Standard Method Performance Requirements (SMPR) purposes or as an extension of a Working Group.
- Consist of a minimum of seven (7) members representing a balance of expert stakeholders. **Quorum is a minimum of 7 members present or 2/3 of the total vetted members, whichever is greater.**
- ERP constituency must be approved by the Official Methods Board (OMB).
- Holds transparent public meetings only.
- Remains in force as long as method in First Action Status.

First Action Official Method Status decision

- Must be made by an ERP constituted or reinstated post 2011-03-28 for First Action Official Method Approval (FAOMA).
- Must be made by an ERP vetted for FAOMA purposes by OMB post 2011-03-28.
- Method adopted by ERP must perform adequately against the SMPR set forth by the stakeholders. Or demonstrate performance or characteristics that meet the scope, applicability and/or claims of the method.
- Method must be adopted by unanimous decision of ERP on first ballot, If not unanimous, negative votes must delineate scientific reasons.
- Negative voter(s) can be overridden by 2/3 of non-negative voting ERP members after due consideration
- Method becomes First Action Official Methods on date when ERP decision is made.
- Methods to be drafted into AOAC format by a knowledgeable AOAC staff member or designee in collaboration with the ERP and method author.
- Report of FAOMS decision complete with ERP report regarding decision including scientific background (references etc) to be published concurrently with method in traditional AOAC publication venues.

Method in First Action Status and Transitioning to Final Action Status

- Further data indicative of adequate method reproducibility (between laboratory) performance to be collected. Data may be collected via a collaborative study or by proficiency or other testing data of similar magnitude.
- Two years maximum transition time (additional year(s) if ERP determines a relevant collaborative study or proficiency or other data collection is in progress).
- Method removed from First Action Official Methods and OMA if no evidence of method use available at the end of the transition time.
- Method removed from First Action Official Methods and OMA if no data indicative of adequate method reproducibility is forthcoming as outlined above at the end of the transition time.
- ERP to recommend Method to Official Final Action Status to the OMB.
- OMB decision on First to Final Action Status

Revised October 2013

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Miscellaneous

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- OMA - Appendix E: Laboratory Quality Assurance
- OMA - Appendix C: Reference Tables

All resources are accessible at
http://www.aoac.org/vmethguidelines.htm

For questions, please contact:
P 301-924-7077 x157 E dmckenzie@aoac.org

About Expert Review Panels (ERPs)

ERP OVERVIEW:

An Expert Review Panel (ERP) is assembled to review and adopt methods as Official First Action. ERPs will track Official Methods for two years or until such time as reproducibility has been demonstrated and cumulative feedback on method use and performance are obtained. ERPs will make a recommendation regarding Final Action method status for all OMAs to the Official Methods Board (OMB).

All ERP members are expected to serve with the highest integrity and without direct or indirect conflicts of interest. A method assignment can last two years. All members of the ERP are expected to actively participate in ERP meetings and to perform duties and reviews in timely fashion. All members should maintain strict adherence to review timelines and deadlines. AOAC staff documents ERP deliberations.

ESTABLISHING AN EXPERT REVIEW PANEL:

- AOAC staff issues a Call for Experts:
  - Based on voluntary consensus standards and methods submitted to AOAC INTERNATIONAL that may meet the standards.
  - Proprietary and sole source method developers submit individual methods to the AOAC Research Institute.
  - Candidates are asked to submit a CV or information that demonstrates expertise to AOAC staff if not already part of a recognized pool of experts.
- AOAC Chief Scientific Officer (CSO) reviews the documentation for the candidates and make recommends a slate for an expert review panel including the chair to the Official Methods Board.
- The candidate list and supporting documentation are forwarded to the Chair of the OMB who will assign the review to at least two OMB members.
- The OMB reviewers will review the candidates for expertise and perceived conflicts of interest and the OMB may then approve the members of the ERP. A Chair for the ERP is also approved.

EXPERT REVIEW PANEL (ERP):

- Review, discuss and demonstrate consensus on methods for Official First Action method status.
- Participate in the publications process of First Action methods.
- Track and discuss feedback all First Action methods for two years.
- Reach and demonstrate consensus on recommendations for Final Action method status.
- Actively participate in the broader stakeholder effort.

ERP CHAIR:

- Lead ERP discussions in the review and adoption of methods for First Action Official Methods.
- Participate in stakeholder panel activities.
- Review and approve ERP report.
- Work with AOAC staff, working groups and other stakeholder panels to ensure a thorough understanding of the standard method performance requirements and the methods to be assessed.
- Implement the OMB First Action to Final Action Guidelines with the ERP members.
- Advise and review First Action methods and post First Action publications.
- Represent the ERP in presenting the ERPs recommendation to the Official Methods Board regarding Final Action method status.

MECHANICS OF AN AOAC EXPERT REVIEW PANEL

- AOAC CSO assigns methods for review to the expert review panel members.
- For each method, 2 ERP members are assigned as primary and secondary reviewers and present at the ERP meeting.
- All members are expected to actively participate and review methods for First Action Official Method status - conducting thorough and prompt review of methods and being prepared to speak on assigned methods at ERP meetings
- The ERP chair and the 2 reviewers for each method are expected to participate in the publications peer review process for First Action methods.
- ERP reviewers track assigned methods that were adopted as First Action Official Methods and update ERP on method use during two year period between First Action and Final Action
  ERP members are expected to participant in the stakeholder panel activities and/or community at large .

- *ERPs can work with topic advisors (aka, subject matter experts)*
- *OMB can recognize a pool of experts from which ERP members can be selected*

Eligibility Criteria for Expert Reviewers

Be a key expert and/or thought leader of the method or priority under consideration.

- Demonstrated knowledge in the appropriate scientific disciplines.
- Demonstrated knowledge regarding data relevant to adequate method performance.
- Demonstrated knowledge of practical application of analytical methods to bona fide diagnostic requirements.

Be approved by the Official Methods Board

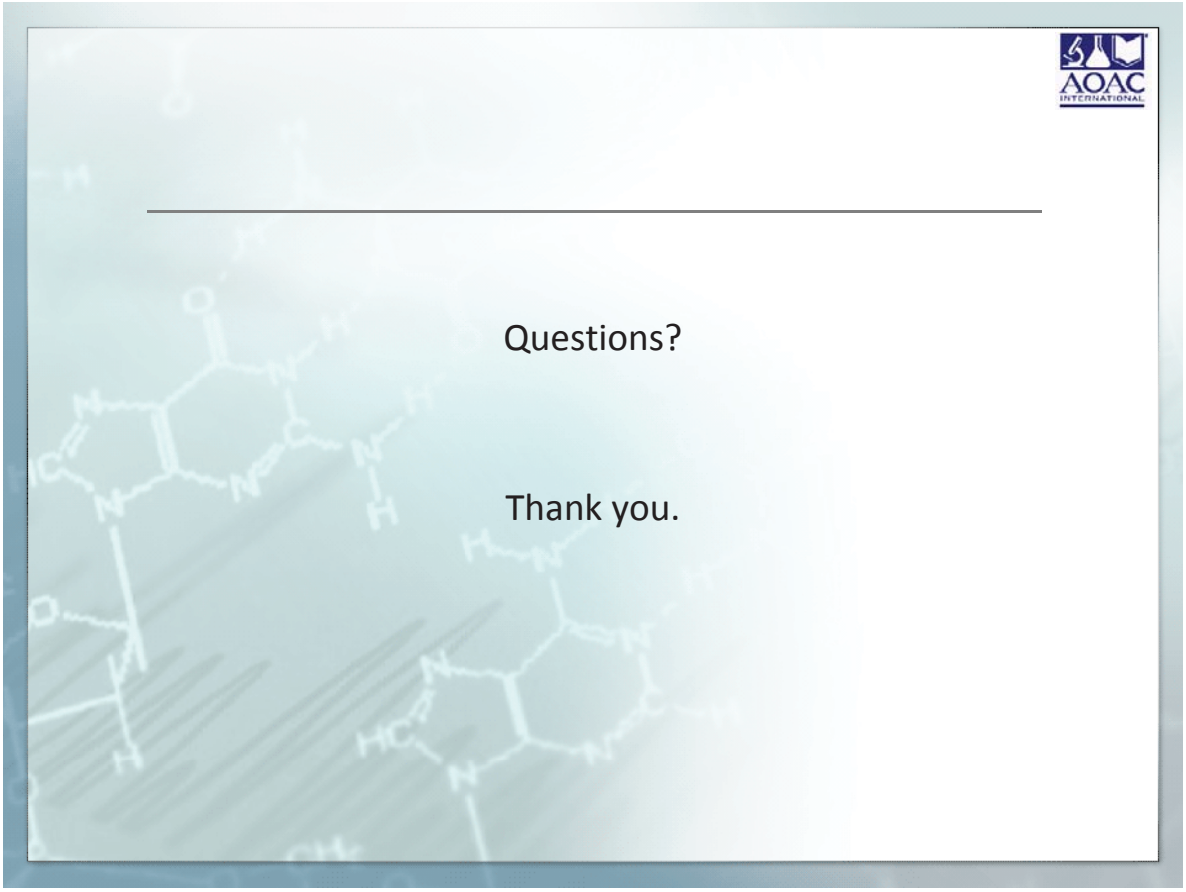
- Qualifications must be clearly described and submitted to AOAC headquarters.

Duties of Expert Reviewers

Members of the Pool of Experts will be called upon to serve on ERPs as needed and to review documents .These documents may include:

- Procedural documents on how methods will be selected and how single laboratory validation studies will be done;
- Methods submitted for consideration as First Action Official Methods;
- Methods submitted for selection for further validation studies;
- Protocols to be used for single laboratory validation studies;
- Selection of methods to be considered for full collaborative studies; and
- Validation study reports

Revised October 2013



Appendix W

POLICY AND PROCEDURES ON VOLUNTEER CONFLICT OF INTEREST

Statement of Policy

While it is not the intention of AOAC INTERNATIONAL (AOAC) to restrict the personal, professional, or proprietary activities of AOAC members nor to preclude or restrict participation in Association affairs solely by reason of such activities, it is the sense of AOAC that conflicts of interest or even the appearance of conflicts of interest on the part of AOAC volunteers should be avoided. Where this is not possible or practical under the circumstances, there shall be written disclosure by the volunteers of actual or potential conflicts of interest in order to ensure the credibility and integrity of AOAC. Such written disclosure shall be made to any individual or group within the Association which is reviewing a recommendation which the volunteer had a part in formulating and in which the volunteer has a material interest causing an actual or potential conflict of interest.

AOAC requires disclosure of actual or potential conflicts of interest as a condition of active participation in the business of the Association. The burden of disclosure of conflicts of interest or the appearance of conflicts of interest falls upon the volunteer.

A disclosed conflict of interest will not in itself bar an AOAC member from participation in Association activities, but a three-fourths majority of the AOAC group reviewing the issue presenting the conflict must concur by secret ballot that the volunteer's continued participation is necessary and will not unreasonably jeopardize the integrity of the decision-making process.

Employees of AOAC are governed by the provision of the AOAC policy on conflict of interest by staff. If that policy is in disagreement with or mute on matters covered by this policy, the provisions of this policy shall prevail and apply to staff as well.

Illustrations of Conflicts of Interest

1. A volunteer who is serving as a committee member or referee engaged in the evaluation of a method or device; who is also an employee of or receiving a fee from the firm which is manufacturing or distributing the method or device or is an employee of or receiving a fee from a competing firm.

2. A volunteer who is requested to evaluate a proposed method or a related collaborative study in which data are presented that appear detrimental (or favorable) to a product distributed or a position supported by the volunteer's employer.

3. A referee who is conducting a study and evaluating the results of an instrument, a kit, or a piece of equipment which will be provided gratis by the manufacturer or distributor to one or more of the participating laboratories, including his or her own laboratory, at the conclusion of the study.

4. Sponsorship of a collaborative study by an interest (which may include the referee) which stands to profit from the results; such sponsorship usually involving the privilege granted by the investigator to permit the sponsor to review and comment upon the results prior to AOAC evaluation.

5. A volunteer asked to review a manuscript submitted for publication when the manuscript contains information which is critical of a proprietary or other interest of the reviewer.

The foregoing are intended as illustrative and should not be interpreted to be all-inclusive examples of conflicts of interest AOAC volunteers may find themselves involved in.

Do's and Don't's

Do avoid the appearance as well as the fact of a conflict of interest.

Do make written disclosure of any material interest which may constitute a conflict of interest or the appearance of a conflict of interest.

Do not accept payment or gifts for services rendered as a volunteer of the Association without disclosing such payment or gifts.

Do not vote on any issue before an AOAC decision-making body where you have the appearance of or an actual conflict of interest regarding the recommendation or decision before that body.

Do not participate in an AOAC decision-making body without written disclosure of actual or potential conflicts of interest in the issues before that body.

Do not accept a position of responsibility as an AOAC volunteer, without disclosure, where the discharge of the accepted responsibility will be or may appear to be influenced by proprietary or other conflicting interests.

Procedures

Each volunteer elected or appointed to an AOAC position of responsibility shall be sent, at the time of election or appointment, a copy of this policy and shall be advised of the requirement to adhere to the provisions herein as a condition for active participation in the business of the Association. Each volunteer, at the time of his or her election or appointment, shall indicate, in writing, on a form provided for this purpose by AOAC, that he or she has read and accepts this policy.

Each year, at the spring meeting of the AOAC Board of Directors, the Executive Director shall submit a report certifying the requirements of this policy have been met; including the names and positions of any elected or appointed volunteers who have not at that time indicated in writing that they have accepted the policy.

Anyone with knowledge of specific instances in which the provisions of this policy have not been complied with shall report these instances to the Board of Directors, via the Office of the Executive Director, as soon as discovered.

* * * * * *

Adopted: March 2, 1989
Revised: March 28, 1990
Revised: October 1996
Reviewed by outside counsel March 2000 (Fran Dwornik) and found to be current and relevant

Appendix U

ANTITRUST POLICY STATEMENT AND GUIDELINES

Introduction

It is the policy of AOAC INTERNATIONAL (AOAC) and its members to comply strictly with all laws applicable to AOAC activities. Because AOAC activities frequently involve cooperative undertakings and meetings where competitors may be present, it is important to emphasize the on-going commitment of our members and the Association to full compliance with national and other antitrust laws. This statement is a reminder of that commitment and should be used as a general guide for AOAC and related individual activities and meetings.

Responsibility for Antitrust Compliance

The Association's structure is fashioned and its programs are carried out in conformance with antitrust standards. However, an equal responsibility for antitrust compliance -- which includes avoidance of even an appearance of improper activity -- belongs to the individual. Even the appearance of improper activity must be avoided because the courts have taken the position that actual proof of misconduct is not required under the law. All that is required is whether misconduct can be inferred from the individual's activities.

Employers and AOAC depend on individual good judgment to avoid all discussions and activities which may involve improper subject matter and improper procedures. AOAC staff members work conscientiously to avoid subject matter or discussion which may have unintended implications, and counsel for the Association can provide guidance with regard to these matters. It is important for the individual to realize, however, that the competitive significance of a particular conduct or communication probably is evident only to the individual who is directly involved in such matters.

Antitrust Guidelines

In general, the U.S. antitrust laws seek to preserve a free, competitive economy and trade in the United States and in commerce with foreign countries. Laws in other countries have similar objectives. Competitors (including individuals) may not restrain competition among themselves with reference to the price, quality, or distribution of their products, and they may not act in concert to restrict the competitive capabilities or opportunities of competitors, suppliers, or customers.

Although the Justice Department and Federal Trade Commission generally enforce the U.S. antitrust laws, private parties can bring their own lawsuits. Penalties for violating the U.S. and other antitrust laws are severe: corporations are subject to heavy fines and injunctive decrees, and may have to pay substantial damage judgments to injured competitors, suppliers, or customers. Individuals are subject to criminal prosecution, and will be punished by fines and imprisonment. Under current U.S. federal sentencing guidelines, individuals found guilty of bid rigging, price fixing, or market allocation must be sent to jail for at least 4 to 10 months and must pay substantial minimum fines.

Since the individual has an important responsibility in ensuring antitrust compliance in AOAC activities, everyone should read and heed the following guidelines.

1. Don't make any effort to bring about or prevent the standardization of any method or product for the purpose or intent of preventing the manufacture or sale of any method or product not conforming to a specified standard
2. Don't discuss with competitors your own or the competitors' prices, or anything that might

affect prices such as costs, discounts, terms of sale, distribution, volume of production, profit margins, territories, or customers.

3. Don't make announcements or statements at AOAC functions, outside leased exhibit space, about your own prices or those of competitors.

4. Don't disclose to others at meetings or otherwise any competitively sensitive information.

5. Don't attempt to use the Association to restrict the economic activities of any firm or any individual.

6. Don't stay at a meeting where any such price or anti-competitive talk occurs.

7. Do conduct all AOAC business meetings in accordance with AOAC rules. These rules require that an AOAC staff member be present or available, the meeting be conducted by a knowledgeable chair, the agenda be followed, and minutes be kept.

8. Do confer with counsel before raising any topic or making any statement with competitive ramifications.

9. Do send copies of meeting minutes and all AOAC-related correspondence to the staff member involved in the activity.

10. Do alert the AOAC staff to any inaccuracies in proposed or existing methods and statements issued, or to be issued, by AOAC and to any conduct not in conformance with these guidelines.

Conclusion

Compliance with these guidelines involves not only avoidance of antitrust violations, but avoidance of any behavior which might be so construed. Bear in mind, however, that the above antitrust laws are stated in general terms, and that this statement is not a summary of applicable laws. It is intended only to highlight and emphasize the principal antitrust standards which are relevant to AOAC programs. You must, therefore, seek the guidance of either AOAC counsel or your own counsel if antitrust questions arise.

Adopted by the AOAC Board of Directors: September 24, 1989
Revised: March 11, 1991
Revised October 1996

Appendix V

POLICY ON THE USE OF THE ASSOCIATION NAME, INITIALS, IDENTIFYING INSIGNIA, LETTERHEAD, AND BUSINESS CARDS

Introduction

The following policy and guidelines for the use of the name, initials, and other identifying insignia of AOAC INTERNATIONAL have been developed in order to protect the reputation, image, legal integrity and property of the Association.

The name of the Association, as stated in its bylaws, is "AOAC INTERNATIONAL". The Association is also known by its initials, AOAC, and by its logo, illustrated below, which incorporates the Association name and a representation of a microscope, book, and flask. The AOAC logo is owned by the Association and is registered with the U.S. Patent and Trademark Office.

The full Association insignia, illustrated below, is comprised of the logo and the tagline, "The Scientific Association Dedicated to Analytical Excellence," shown below. The typeface used is Largo. The AOAC tagline is owned by the Association and is registered with the U.S. Patent and Trademark office.

The Scientific Association Dedicated to Analytical Excellence®

Policy

Policy on the use of the Association's name and logo is established by the AOAC Board of Directors as follows:

> "The Board approves and encourages reference to the Association by name, either as AOAC INTERNATIONAL or as AOAC; or reference to our registered trademark, AOAC®, in appropriate settings to describe our programs, products, etc., in scientific literature and other instances so long as the reference is fair, accurate, complete and truthful and does not indicate or imply unauthorized endorsement of any kind.
>
> The insignia (logo) of AOAC INTERNATIONAL is a registered trade and service mark and shall not be reproduced or used by any person or organization other than the Association, its elected and appointed officers, sections, or committees, without the prior written permission of the Association. Those authorized to use the AOAC INTERNATIONAL insignia shall use it only for

the purposes for which permission has been specifically granted.

The name and insignia of the Association shall not be used by any person or organization in any way which indicates, tends to indicate, or implies AOAC official endorsement of any product, service, program, company, organization, event or person, endorsement of which, has not been authorized by the Association, or which suggests that membership in the Association is available to any organization."

The Executive Director, in accordance with the above stated policy, is authorized to process, approve, fix rules, and make available materials containing the Association name and insignia.

It should be noted that neither the Association's name nor its insignia nor part of its insignia may be incorporated into any personal, company, organization, or any other stationery other than that of the Association; nor may any statement be included in the printed portion of such stationery which states or implies that an individual, company, or other organization is a member of the Association.

Instructions

1. Reproduction or use of the Association name or insignia requires prior approval by the Executive Director or his designate.

2. Association insignia should not be altered in any manner without approval of the Executive Director or his designate, except to be enlarged or reduced in their entirety.

3. Artwork for reproducing the Association name or insignia, including those incorporating approved alterations, will be provided on request to those authorized to use them (make such requests to the AOAC Marketing Department). Examples of the types of alterations that would be approved are inclusion of a section name in or the addition of an officer's name and address to the letterhead insignia.

4. When the Association name is used without other text as a heading, it should, when possible, be set in the Largo typeface.

5. Although other colors may be used, AOAC blue, PMS 287, is the preferred color when printing the AOAC insignia, especially in formal and official documents. It is, of course, often necessary and acceptable to reproduce the insignia in black.

6. Do not print one part of the logo or insignia in one color and other parts in another color.

7. The letterhead of AOAC INTERNATIONAL shall not be used by any person or organization other than the Association, elected and appointed officers, staff, sections, or committees; except by special permission.

   Correspondence of AOAC official business should be conducted using AOAC letterhead. However, those authorized to use AOAC letterhead shall use it for official AOAC business only.

   Copies of all correspondence using AOAC letterhead or conducting AOAC official business,

whether on AOAC letterhead or not, must be sent to the appropriate office at AOAC headquarters.

8. AOAC INTERNATIONAL business cards shall not be used by any person or organization other than the Association, its staff, and elected officials, except by special permission.

   Those authorized to use AOAC business cards shall use them for official AOAC business only and shall not represent themselves as having authority to bind the Association beyond that authorized.

Sanctions

1. Upon learning of any violation of the above policy, the Executive Director or a designate will notify the individual or organization that they are in violation of AOAC policy and will ask them to refrain from further misuse of the AOAC name or insignia.

2. If the misuse is by an Individual Member or Sustaining Member of the Association, and the misuse continues after notification, the Board of Directors will take appropriate action.

3. If continued misuse is by a nonmember of the Association or if a member continues misuse in spite of notification and Board action, ultimately, the Association will take legal action to protect its property, legal integrity, reputation, and image.

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Adopted by the AOAC Board of Directors: September 24, 1989
Revised: June 13, 1991; February 26, 1992; March 21, 1995; October 1996