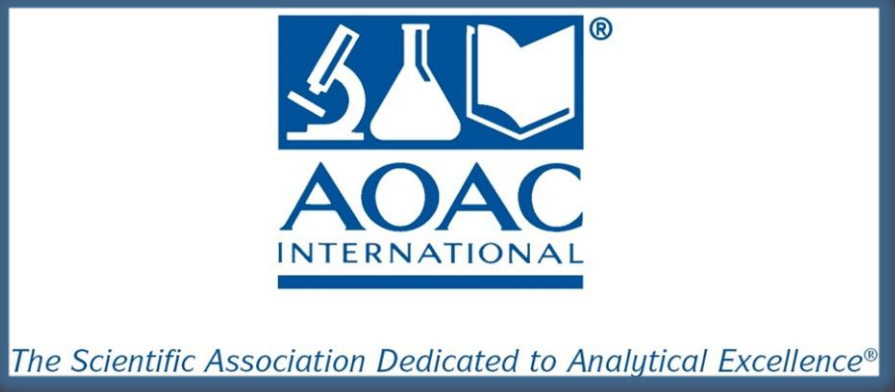


AOAC INTERNATIONAL Presents…

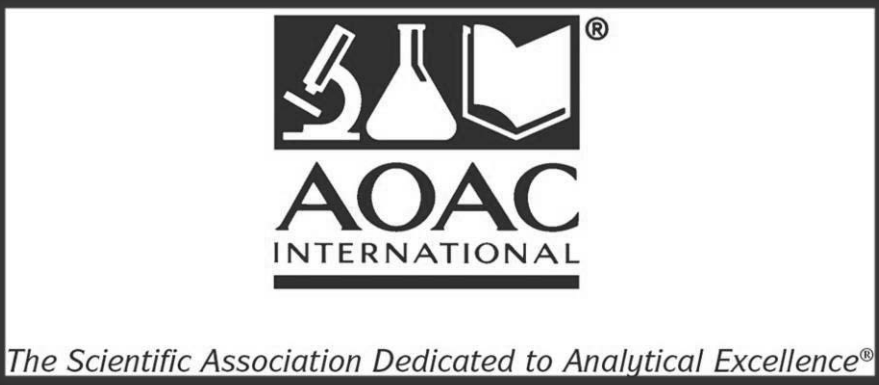
the Stakeholder Panel on Strategic Food Analytical Methods

(SPSFAM)

SUNDAY, SEPTEMBER 18, 2016, 8:30 a.m.
Room: San Antonio B

DALLAS SHERATON HOTEL
400 NORTH OLIVE STREET
DALLAS, TEXAS, UNITED STATES

contact: spds@aoac.org



AOAC INTERNATIONAL Presents…

the Stakeholder Panel on Strategic Food Analytical Methods

(SPSFAM)

SUNDAY, SEPTEMBER 18, 2016, 8:30 a.m.
Room: San Antonio B

DALLAS SHERATON HOTEL
400 NORTH OLIVE STREET
DALLAS, TEXAS, UNITED STATES

contact: spds@aoac.org

Stakeholder Panel on Strategic Food Analytical Methods - Chair Biography

Co-Chair, SPSFAM

Erik Konings

Nestle Research Center

Erik Konings studied higher professional laboratory education with majors in analytical and clinical chemistry. After graduating in 1984, he started his professional career at the then called Food Inspection Service in Maastricht, the Netherlands. In 2001 he completed his PhD study “Dietary folates in human nutrition” at Maastricht University. During this study, he obtained an MSc-degree in epidemiology. He is (co)author of more than 30 scientific publications.

In September 2008 he started at the European Food Safety Authority (EFSA) in Parma, Italy, for a secondment as Scientific Officer at the Data Collection and Exposure Unit, and from there accepted, in June 2009, a position at the Nestlé Research Centre in Lausanne, Switzerland, currently in a role as Food Safety & Quality expert. He is active in several Standard Developing Organisations as AOAC INTERNATIONAL (Past-President), ISO, CEN, and IDF, and participates in the Codex Committee on Methods of Analysis and Sampling (CCMAS).

PRESENTER BIOS

SUSAN AUDINO, Audino & Associates, LLC

Susan Audino obtained her PhD in Chemistry with an analytical chemistry major, physical and biochemistry minor areas. Susan was the recipient of NSF Chemometric Graduate Fellowship and was a visiting scientist at NIST where she completed her graduate research. She currently owns and operates a consulting firm to service chemical and biological laboratories, is an A2LA Lead Assessor and Instructor, and serves as a Board Member for the Center for Research on Environmental Medicine in Maryland. She is also serving as Quality Director for several laboratories and has worked with a variety of laboratories to establish and/or improve their quality management systems.

Susan has been studying the chemistry and applications of cannabinoids and provides scientific and technical guidance to medical marijuana dispensaries, testing laboratories, medical personnel, and regulatory agencies. Dr. Audino's interest most directly involves marijuana/cannabis consumer safety and protection, and promotes active research towards the development of Official Test methods specifically for this industry. In addition to serving on Expert Review Panels, she has been working closely with AOAC to develop interest and movement toward the development of scientifically sound methodologies for the cannabis sector. Prior to her study of chemistry, Dr. Audino received advanced degrees and practiced psychology for more than a decade.

THIERRY DELATOUR, Nestlé

Dr. Delatour is a Lead Scientist at Nestlé Research Centre in Lausanne, Switzerland where he specializes in response in analytical chemistry to emerging issues and crises. Prior to this, he was a Group Leader at Nestlé Research Centre where he managed a team of experts dedicated to the development of analytical methods in the Quality & Safety Department. These methods have been implemented in R&D Centre, PTC and NQAC. Dr. Delatour obtained his Ph.D. from Centre d'Etudes Nucléaires de Grenoble in France, a Master of Advanced Studies at Université Joseph Fourier, and an Engineer in Chemistry Degree at Institut de Chimie et Physique Industrielles.

BRIAN SCHANEBERG, Starbucks Coffee Co.

Brian Schaneberg, Ph.D., is the Global Scientific & Regulatory Affairs Director for Starbucks Coffee Company. Brian has over 15 years of natural products experience in the area of dietary supplements and herbals. Brian was also the Quality & Food Saftey and Scientific & Regulatory Affairs Director for Mars Botanical, a division of Mars, Inc. focusing on cocoa flavanol science and products. Before Mars Botanical, he was the Director of Technical Services at ChromaDex, Inc. in Irvine, California and was an Associate Research Scientist at the National Center for Natural Products Research at the University of Mississippi under the guidance of Dr. Ikhlas Khan, in a position funded by the US FDA for the development of methods to ensure the quality and safety of botanicals and dietary supplements. Over the years, Brian has worked closely with trade groups, industry, academia and government leaders. He has been a member of various review committees including NIH grants, analytical validation ERPs at AOAC and the Registry of Carcinogens. Brian also had the pleasure of holding an adjunct faculty position at the University of Colorado, Denver, advising a student that received his MS in Analytical Chemistry isolating phytochemicals and developing analytical testing procedures for Horse Chestnut. Brian has a Ph.D. in Organic Chemistry from Virginia Commonwealth University and a B.A. in Chemistry with a minor in Biology from Central College in Iowa. He has authored or co-authored more than 50 publications and presentations.

The Scientific Association Dedicated to Analytical Excellence®

Stakeholder Panel on Strategic Food Analytical Methods (SPSFAM)

Chair: Erik Konings, Nestlé,

September 18, 2016 | 8:30AM – 12:00PM CT

Registration Opens at 7:30 a.m.

Sheraton Dallas Hotel| 400 North Olive Street| Dallas, TX, USA
Conference Room: San Antonio B

A G E N D A

I. Welcome and Introductions (8:30 a.m. – 8:50 a.m.)
Jim Bradford, AOAC; Norma Hill, AOAC President; Erik Konings, Nestlé, SPSFAM Chair
   a. Policies and Procedures
   b. Approval of March 24, 2016 Minutes
   c. Working Group Initiative Success Stories

II. ERP Updates (8:50 a.m. – 9:00 a.m.)
Erik Konings, Nestlé, SPSFAM Chair

III. Working Group Launch Presentation: Cannabis Potency * (9:00 a.m. - 10:00 a.m.)
SPSFAM Working Group on Cannabis Potency - Chair: Susan Audino, Audino and Associates LLC

[BREAK]

IV. Working Group Launch Presentation: Proanthocyanidins in Cranberry Products* (10:15 a.m. – 11:15 a.m.)
SPSFAM Working Group on Proanthocyanidins in Cranberry Products - Chair: Brian Schaneberg, Starbucks

V. International Stakeholder Panel on Alternative Methodology (ISPAM) Update (11:15 a.m. – 11:25 a.m.)
Erik Konings, Nestlé, SPSFAM Chair

VI. Emerging Contaminants and Multi-Residue Analysis of Veterinary Drugs (11:25 a.m. – 11:55 a.m.)
Thierry Delatour, Nestlé, Member of Chemical Contaminants and Residues in Food Community

VII. Other Business and Next Steps (11:55 a.m. – 12:00 p.m.)
Erik Konings, Nestlé, SPSFAM Chair

VIII. Adjourn

**Item requires a vote*

AOAC Stakeholder Panel on Strategic Food Analytical Methods: Stakeholder Panel Meeting

Meeting Minutes
Monday, March 14, 2015; 1:00 p.m. – 5:00 p.m. ET

Attendees:

Erik Konings, Nestlé Research Center (SPSFAM Chair)
Dave Almy, Neogen Corporation
Brad Barrett, GERSTEL
DeAnn Benesh, 3M Food Safety
Tim Beshore, Self Employed
Patrick Bird, Q Laboratories
Joe Boison, Candian Food Inspection Agency
Michelle Briscoe, Brooks Applied Labs
Mike Clark, Bio-Rad Laboratories
Bob Clifford, Shimadzu Scientific Instruments
Sean Conklin, US FDA
Tim Croley, US FDA
Erin Crowley, Q Laboratories
Hannah Crum, Kombucha Brewers Institute
David Cunningham, Ocean Spray Cranberries
Katherine Fielder, US FDA
Andrew Fussell, PANalytics
Russell Gerads, Brooke Applied Labs
Brendon Gill, Fonterra Cooperative Group
Nicole Hart, Agilent Technologies
Norma Hill, US Treasury (Retired)
Greg Hostettler, PBM/Perrigo Nutritionals
Min Huang, Frontage
Greg Jaudzems, Nestlé
George Joseph, AsureQuality
Kristie Laurvick, USP
Haiyan Lin, Ocean Spray Cranberries
Sookwang Lee, US FDA
Ferry Maniei, The Coca-Cola Company
Vicky Manti, Danone Nutricia
Elaine Marley, R-Biopharm
Katerina Mastovska, Covance Laboratories
Josh Messerly, Eurofins
Paul Milne, Keurig Green Mountain
Bill Mindak, US FDA
Deepali Mohindra, Thermo Fisher Scientific
Jenny Nelson, Agilent Technologies
Lawrence Pacquette, Abbott Nutrition
Miguel Pagan, Agilent Technologies
Christine Parker, US FDA
Melissa Phillips, US NIST
Bert Popping, Mérieux NutriSciences
Guenther Raffler, Eurofins
Rick Reba, Nestlé
Catherine Rimmer, US NIST
Shauna Roman, Reckitt Benckiser
Joe Romano, Waters Corporation
André Schreiber, SCIEX
Jenny Scifres, USDA FSIS
Brooke Schwartz, Brooke Schwartz Consulting
Christopher Smith, The Coca-Cola Company
Kathy Stenerson, MilliporeSigma
Cheryl Stephenson, Eurofins
Joan Stevens, Agilent Technologies
Darryl Sullivan, Covance Laboratories
John Szpylka, Mérieux NutriSciences
Steve Tennyson, Perrigo Nutritionals
Joe Thompson, Abbott Nutrition
Justin Trout, Health-Ade Kombucha
Socrates Trujillo, US FDA
Sue Wang, ITRI
Wayne Wargo, Abbott Nutrition
Laura Wood, US NIST
David Woolard, Eurofins
Xianli Wu, USDA
Jason Wubben, Archer Daniels Midland Company
Dorothy Yang, Agilent Technologies
Jinchaun Yang, Waters Corporation
Chunyan Zhang, Abbott Nutrition
Yao Zhou, SHCIQ
Jerry Zweigenbaum, Agilent Technologies

AOAC Staff:

Jim Bradford
Scott Coates
Christopher Dent
Jonathan Goodwin
Arlene Fox
Dawn Frazier
Nora Marshall
Deborah McKenzie
Tien Milor
La'Kia Phillips
Joyce Schumacher
Robert Rathbone

Meeting Minutes

I. Welcome and Introductions

AOAC Executive Director, Dr. Jim Bradford opened the meeting and led introductions before introducing the President of AOAC INTERNATIONAL, Norma Hill. Hill shared brief remarks before introducing SPSFAM Chair, Dr. Erik Konings. Konings requested motions to approve the September 27, 2015 Meeting Minutes.

MOTION by Boison / Wubben to approve the September 27, 2015 SPSFAM Meeting Minutes as presented. 15 in favor, 0 opposed, 0 abstain.
The motion passed.

Konings also advised that voting members have been assigned by organization rather than by individual. Organizations with a seat at the voting table may determine who will represent their interests at this meeting.

II. Heavy Metals Expert Review Panel Updates

Konings introduced Reba, Chair of the AOAC Expert Review Panel (ERP) for SPSFAM Heavy Metal Methods. Reba explained that five (5) methods were submitted in response to the call for methods to meet AOAC SMPR 2015.006, *Quantitation of Arsenic Species in Selected Food and Beverages.* Reba advised that the ERP met earlier in the day and approved one method for First Action *Official Methods*^{SM} satus. Suggestions were made for the unapproved methods. Furthermore, Reba shared the consensus of the ERP regarding methods meeting the LOQ for rice and that the stakeholder panel may want to consider re-engaging the AOAC SPSFAM Heavy Metals Working Group to revisit the LOQ for rice.

Reba also shared that the First Action method for Total Heavy Metals in Food, AOAC 2015.01 is nearly ready to move forward with reproducibility assessment and that there are 16-18 labs planning to contribute to the assessment.

III. Glyphosate Update

Konings explained that at the last SPSFAM meeting, there was a presentation on the potential for a Glyphosate Working Group, which was identified as a concern for many stakeholders. Since then, AOAC staff has attempted to secure the funding required for this project. Because funding has not been secured, SPSFAM will put this project on hold. Konings advised all to contact AOAC staff if they are interested in supporting a working group.

IV. SMPR Presentation: Kombucha

Konings introduced Crum, who took the floor with a presentation[1] on the work of the Kombucha Working Group. After reviewing the draft standard for Quantitation of Ethanol in Kombucha and the reconciled comments, Crum made a motion for SPSFAM to approve the draft SMPR for Detection of Ethanol in Kombucha as presented, and Szpylka seconded the motion. Discussion on the analytical range followed the motion. The group agreed to change the upper end of the range from 2.8% ABV to 2.0% ABV.

MOTION to approve the SMPR for Detection of Ethanol in Kombucha (Crum / Szpylka)
13 in favor, 0 against, 2 abstain. The motion passed.

Konings thanked Crum and advised the panel that AOAC will issue a Call for Methods with the expectation to hold an Expert Review Panel for Kombucha methods in September 2016.

V. SMPR Presentation: Allergens

Konings invited Paez to take the floor. Paez provided a presentation[2] on the progress of the Allergens working group. Paez explained that although the original fitness for purpose called for an SMPR for detection of eight (8) allergens, this has been reduced by the working group and the SMPR developed focuses on detection of peanut, hazelnut, whole egg, and milk. Eight were considered too broad a scope for this SMPR. However, the need for the other SMPRs for the other allergens remains and Paez encouraged anyone who may be able to help fund that project to contact AOAC staff. Paez invited AOAC CSO, Scott Coates to review the draft SMPR. After reviewing the SMPR, Coates mentioned that there were twenty-four (24) comments were submitted for this SMPR prior to this meeting and all have been addressed – details are in the meeting book. Paez then motioned for SPSFAM to approve the SMPR for the Detection and Quantitation of Selected Food Allergens as presented and Boison seconded the motion. After a discussion on reference materials, the group agreed to change the heading for reference materials to “examples of potential reference materials” and also to remove the reference material “nonfat milk powder.” Furthermore, all instances of Limit of Quantitation (LOQ) were replaced with MQL (method quantitation limit). Paez revised the motion.

MOTION to accept the SMPR for Detection and Quantitation of Selected Food Allergens as amended at this meeting (Paez /Boison).
11 in favor, 2 opposed, 2 abstain. The motion passed.

VI. Next Steps and Adjourn

Konings then reviewed next steps. There will be a call for methods for both Kombucha and allergens with an ERP tentatively taking place in September at the AOAC Annual Meeting in Dallas. Konings

[1] Kombucha SMPR Presentation
[2] Allergens SMPR Presentation

also reminded the group that if there is interest in pursuing more allergens, please contact AOAC staff regarding support for this effort.

Konings adjourned the meeting at approximately 4:00 p.m. ET.

MARCH 14, 2016 SPSFAM MEETING: ACTION ITEMS	
Action	**Owner**
Move approved SMPRs to publication stage	AOAC Staff
Issue call for methods to meet SMPRs for Kombucha and Allergens	AOAC Staff

Attachments:

Attachment 1: Kombucha SMPR Presentation (Crum)

Attachment 2: Kombucha SMPR (as approved)

Attachment 2: Allergens SMPR Presentation (Paez)

Attachment 4: Allergens SMPR (as approved)

Cachexia, Cancer, Chronic Pain, Epilepsy, Glaucoma, HIV, AIDS, Multiple Sclerosis, Nausea, ALS, Crohn's, Hepatitis C, Anorexia, Arthritis, Migraine, Parkinson's, Damage to the Nervous Tissue of the Spinal Cord with Objective Neurological Indication of Intractable Spasticity, PTSD, Traumatic Brain Injury, Use of Azidothymidine, Tourette Syndrome, Lupus, Chemotherapy or Radiotherapy, Reflex Sympathetic Dystrophy, Neurofibromatosis, Arnold-Chiari Malformation, Hydrocephalus, Residual Limb Pain, Terminal Illness with a Life Expectancy Under One Year, Hospice Care, Huntington's, Chronic Renal Failure …

If you or someone you know suffers or endures any one of these, you have an interest in the medical marijuana industry and recognize the importance of analytical testing.

Stakeholder Panel on Strategic Food Analytical Methods: Background and Fitness for Purpose for CANNABIS

Susan Audino, PhD
S.A. Audino & Associates, LLC

AOAC International – Dallas, TX
September 18, 2016

Cannabis Advisory Panel

- Susan Audino, Chair
- GW Pharmaceuticals – Peter Gibson
- SC Laboratories – Josh Wurzer
- SCIEX – Paul Winkler
- SPEX – Patricia Atkins
- Sigma Aldrich – Jennifer Claus
- CEM – Bob Lockerman

Medical Cannabis Background

- Medicinal Marijuana is legal in 24 states & D.C.
- Schedule I Drug = “No medicinal value” → Federal Prohibition
- States are self-regulated
- Several require analytical testing
  - Potency
  - Pesticide Residue
  - Microbial
  - Solvent Residue

Medical Cannabis Background

- The PLANT
  - Highly complex herb; heterogeneous within and between
  - More than 400 constituents – approximately 114 are “phyto cannabinoids” which are naturally occurring cannabinoids
  - About a dozen of these have demonstrated medicinal value
  - Only one is psychoactive
  - More than 29 flavonoids
- The CANNABINOIDS
  - All contain carboxylic acid groups that are kicked off with heat
  - Interest in both “acid” and “neutral” compounds
  - Cannabinoid acids are devoid of psychotropic effects

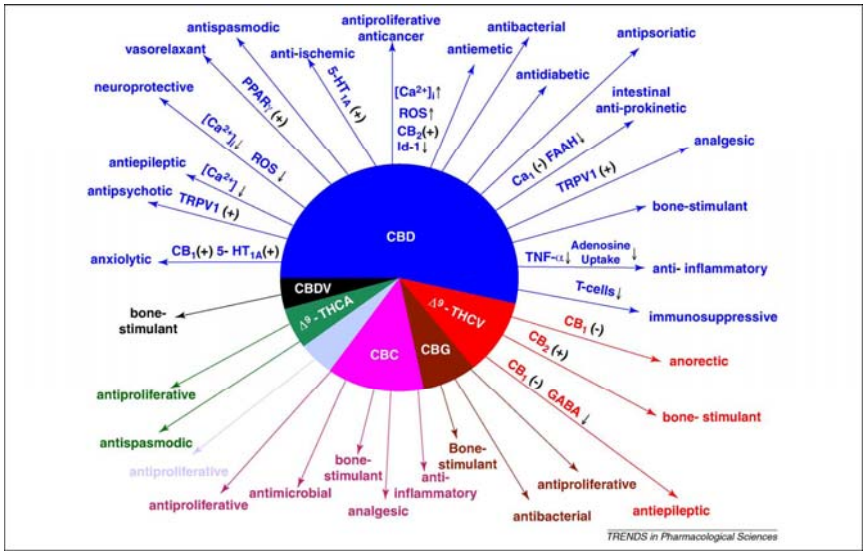
Some Medicinal Applications & Benefits

- Decreases intra-ocular pressure – **Glaucoma**
- Provides some abatement of severe anxiety – **PTSD**
- Reduces seizure activity; in some cases from 300 to 1/week
- Provides suppression of muscle spasms – **Multiple Sclerosis**
- Provides calming effect on the immune system - **Lupus**

Health Effects of Marijuana	THC	THC-A	THC-V	CBN	CBD	CBD-A	CBC	CBC-A	CBG	CBG-A	Benefits
Pain relief	■			■	■		■		■		Analgesis
Reduces inflammation		■			■	■	■		■	■	Anti-inflamatory
Supresses appetite			■								Anoretic
Stimulates appetite	■				■						Appetite stimulant
Reduces vomiting and nausea	■				■						Antimetic
Reduces contractions of small intestine					■						Intestinal antiprokinetic
Relieves anxiety					■						Anxiolytic
Tranquilizing / psychosis management					■						Antipsychotic
Reduces seizures and convulsions		■	■		■						Antiepileptic
Suppresses muscle spasms	■			■	■						Antispasmodic
Aides sleep				■							Anti-insomnia
Reduces efficacy of immune system					■						Immunosuppresive
Reduces blood sugar levels			■		■						Anti-diabetic
Prevents nervous system degeneration					■						Neuroprotective
Treats psoriasis					■						Antipsioratic
Reduces risk of artery blockage					■						Anti-ischemic
Kills or slows bacteria growth					■		■	■	■		Anti-bacterial
Treats fungal infection								■	■		Anti-fungal
Inhibits cell growth in tumours / cancer		■			■	■	■		■		Anti-proliferative

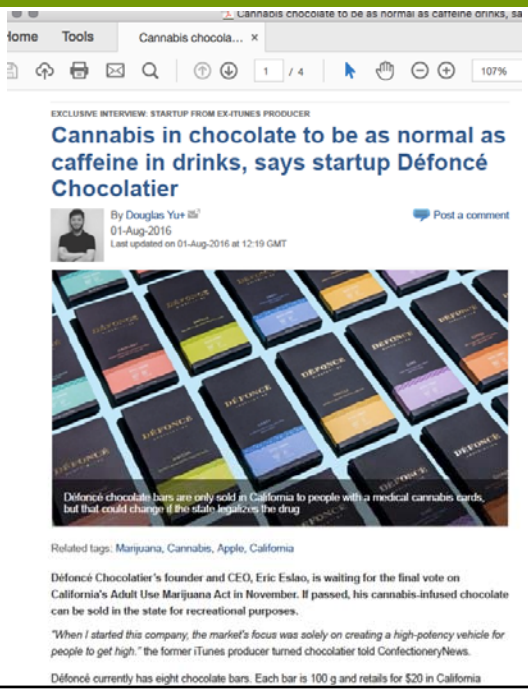
How does this work?

- Endocannabinoid Receptor System (ECS)
- Discovered in mid-1990s and found in every living being except insects.
- Two known receptors (more expected on the horizon)
  - CB1 and CB2
  - CB1: predominantly found in the brain; helps modulate and moderate pain
  - CB2: primarily found in the immune system; has anti-inflammatory properties



Cannabis "Dosing"

- Inhalation: Smoke, Vapors
- Transdermal: Patches, Salves
- Oral: Edibles, Tinctures
- **Most challenging: Edibles**
- **Hottest Topic of the Day: Pesticide Residues**



Cannabis chocolate to be as normal as caffeine drinks, sa

Home Tools Cannabis chocola... ×

1 / 4 107%

EXCLUSIVE INTERVIEW: STARTUP FROM EX-ITUNES PRODUCER

Cannabis in chocolate to be as normal as caffeine in drinks, says startup Défoncé Chocolatier

By Douglas Yu+

01-Aug-2016

Last updated on 01-Aug-2016 at 12:19 GMT

Post a comment

Défoncé chocolate bars are only sold in California to people with a medical cannabis cards, but that could change if the state legalizes the drug

Related tags: Marijuana, Cannabis, Apple, California

Défoncé Chocolatier's founder and CEO, Eric Eslao, is waiting for the final vote on California's Adult Use Marijuana Act in November. If passed, his cannabis-infused chocolate can be sold in the state for recreational purposes.

"When I started this company, the market's focus was solely on creating a high-potency vehicle for people to get high." the former iTunes producer turned chocolatier told ConfectioneryNews.

Défoncé currently has eight chocolate bars. Each bar is 100 g and retails for $20 in California

Food Items & Label Claims

Significance

If edibles are the vehicle for dosing, then knowing what and how much of the analyte is present becomes the single most critical factor.

Reliable and Effective Testing is IMPERATIVE.

What does this mean?

- Producers are making potency and constituent claims.
- How can they be challenged?
- **Consumer Safety**

Analytical Challenges

- COMPLEX MATRIX
  - Raw Plant material
    - Trim
    - Bud
    - Flower
    - Stem
    - Composite




- Heterogeneity
  - Within a single plant
  - Between different plants – same strain or different strains

Analytical Challenges

- **Food Matrices**

– when is cannabis introduced into the product?

- Beginning of process
- Mid-Process
- Topical/surface

- What is the end product?
  - And what/if any loss in cannabis is realized?

Significance and Implications

- The LACK of consensus methods
  - Inadequate testing
  - Inappropriate testing
  - Non-Reproducibility
  - Inherently unreliable
- Constant battle between growers and test labs → SAMPLE SIZE
- Instrumentation – better testing costs more in $$ and time
- Balancing scientific acumen with business

General Analytical Needs

- Potency
  - THC, THCA, THCV
  - CBD, CBDA, CBDV
  - CBG
  - CBN
- Pesticide Residues
- Matrices
  - Raw
  - **Extracts**
  - **Edibles**

General Analytical Needs

- Consensus methods
  - Validated
  - Statistically Sound
  - Reproducible
  - Repeatable
  - Reliable
  - Robust
  - Correct Technology
- Affordable to consumers
- Traditional methodology

Challenges

- Federal Prohibition
- Matrix Effects
- Fiscal concerns:
  - Sample Size
  - Instrumentation
  - Analyst skill set
  - Turn-around-time
  - Qualitative vs. Quantitative
- Pesticides – which ones??

General Methods: US Herbal Pharmacopoeia Monograph

- ***No standardized methods***
- ***Methods are outlined but seem to lack validation data.***

- GC -FID: quantitation of phytocannabinoids
- ICP-MS: Metals (Ar, Cd, Cr, Pb, Hg)
- GC/HPLC: Pesticides
  - Refers to FDA Pesticide Analytical Manual
- TLC

No /Inconsistent Regulatory Guidance

- NO Federal Guidance: ~~FDA~~ ~~EPA~~ ~~USDA~~
- States are self regulating and developing their own sets of standards and requirements
  - ISO/IEC 17025
  - TNI
  - Other
  - None
- State Oversight
  - DOH
  - Agriculture
  - Commissions
  - Other

Sense of Urgency

- In the interest of *consumer safety*, an advisory panel has formed and is committed to developing consensus methods for specific use in the cannabis industry.
- The field is large; our initial objective(s) is to systematically target most urgent needs which may include:
  - Determining the most cost efficient and scientifically sound sample preparation method(s)
  - Determining potency of the most significant phyto-cannabinoids
    - For example: THC, THCA, THCV, CBD, CBDA, CBDV, CBN, CBG
  - Determining pesticide residues
  - Determining solvent residues

Proposed Fitness for Purpose

~ Standard Methods Performance Requirements (SMPRs) for quantitative methods for various measurements of cannabinoids in raw materials and extracts ~

Next Steps

- Form Working Group(s) of interested and capable personnel with commitment to solve this problem.

- Advantages
  - Close work with highly reputable analysts
  - Be a trend setter!
  - Be among the first to establish critical methods for the benefit of consumer safety

QUESTIONS & DISCUSSION

Susan Audino,PhD

Susan.Audino@gmail.com
410.459.9208

Stakeholder Panel on Strategic Food Analytical Methods: Background and Fitness for Purpose for *Proanthocyanidins in Cranberry Products*

Brian Schaneberg
Dallas, TX
September 18, 2016

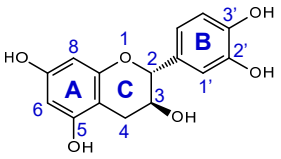
Background on the Analyte

- Cranberry juice has been used traditionally for the treatment and prevention of urinary tract infections
- Effectiveness first demonstrated by Avorn, et. al. in a randomized, double-blind, placebo-controlled study in 1994
- Sobota first proposed a bacterial (*E. Coli*) anti-adhesion (uroepithelial cell) mechanism for cranberry in 1984
- Howell, et. al. used an anti-adhesion bioassay directed fractionation of cranberry juice and identified A-Type proanthocyanidins as the active components in 1998
- Feliciano, et. al. have also shown A-type PACs inhibited gut colonization of uropathogenic *E. coli* in 2013

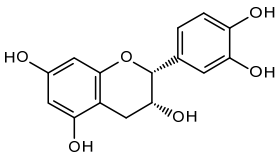
Structures of PACs

Mixtures of oligomers and polymers composed of flavan-3-ols

Flavan-3-ols

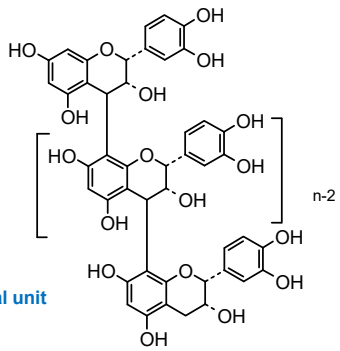


(+)-Catechin



(-)-Epicatechin

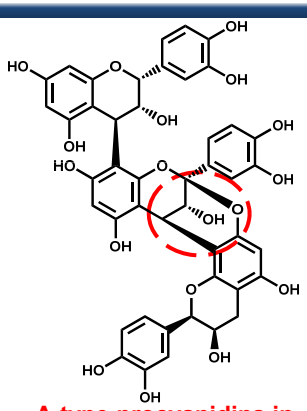
Oligomeric and polymeric PACs



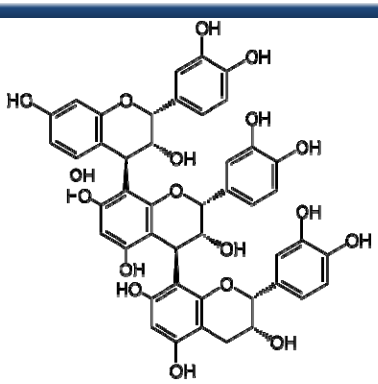
- ✓ DP: degree of polymerization
- ✓ Oligomers: DP 2-10
- ✓ Polymers: DP＞10
- ✓ **Epicatechin is the primary constituent monomer in cranberry PACs**

3

Cranberry PACs are unique



A-type procyanidins in Cranberries



B-type procyanidins in other fruits

- ✓ **95% of cranberry PAC oligomers contain 1 or more A-type bonds.**
- ✓ **26% of cranberry PAC oligomers contain 2 or more A-type bonds.**

Background on the Analyte (continued)

- Cranberries containing proanthocyanidins are typically not consumed “as is” due to their naturally low sugar content and high acid content, compared to common fruits such as apples and grapes, and instead are used in a wide variety or ways or products such as beverages, sauces and relishes, dried cranberries, snacks, ingredients (juice concentrate, dried powders, extracts) and dietary supplements
- In addition to urinary tract health, proanthocyanidins contribute to the antioxidant activity exhibited by cranberry and other fruits rich in polyphenolic compounds

Significance (or implications)

- Companies want to market products (foods, dietary supplements, medical foods and botanical drugs) that can be formulated to deliver effective and consistent concentrations of proanthocyanidins to consumers
- Need to standardize products used by researchers for clinical studies
- Companies need to evaluate the impact of processing on and the shelf-life of proanthocyanidins in various products

General Analytical Needs

Recognize two basic analytical needs:

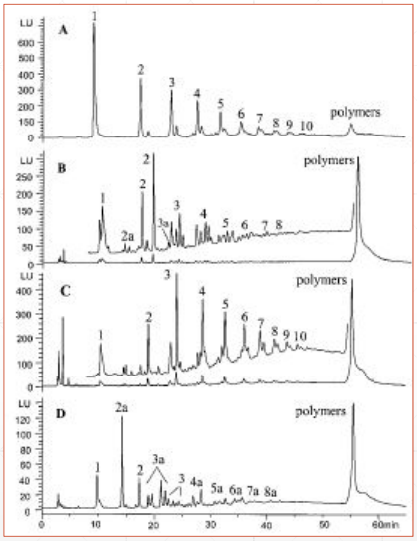
1. Quantitative QC method to support product manufacture
   a) Quick
   b) Easy
2. Qualitative method to verify authenticity

Challenges

- Recognize four primary challenges in the analysis of cranberry proanthocyanidins
  1. Analyte heterogeneity and complexity
     a) Not a single compound
     b) Wide range of DP and Isomers
     c) Differentiating structural characteristic (A-type versus B-Type)
  2. Range of solubility impacts sample preparation and analysis
  3. Lack of standards
     a) Results differences between methods
  4. Achieving methodology consensus

Existing Methods (Official)

- Two AOAC methods of analysis (2012.24 and 2013.03)
- Applicable to cocoa based matrices
- NP-HPLC Chromatography
- Quantify procyanidins from DP1-10 based on Fluorescence RF



Cocoa

Lowbush blueberry

Sorghum

Cranberry

Existing Methods (Official)

- European Pharmacopeia
- Dried hawthorne berry assay procedure (assay minimum 1.0%)
- Colorimetric method
- Reports procyanidin content expressed as cyanidin chloride

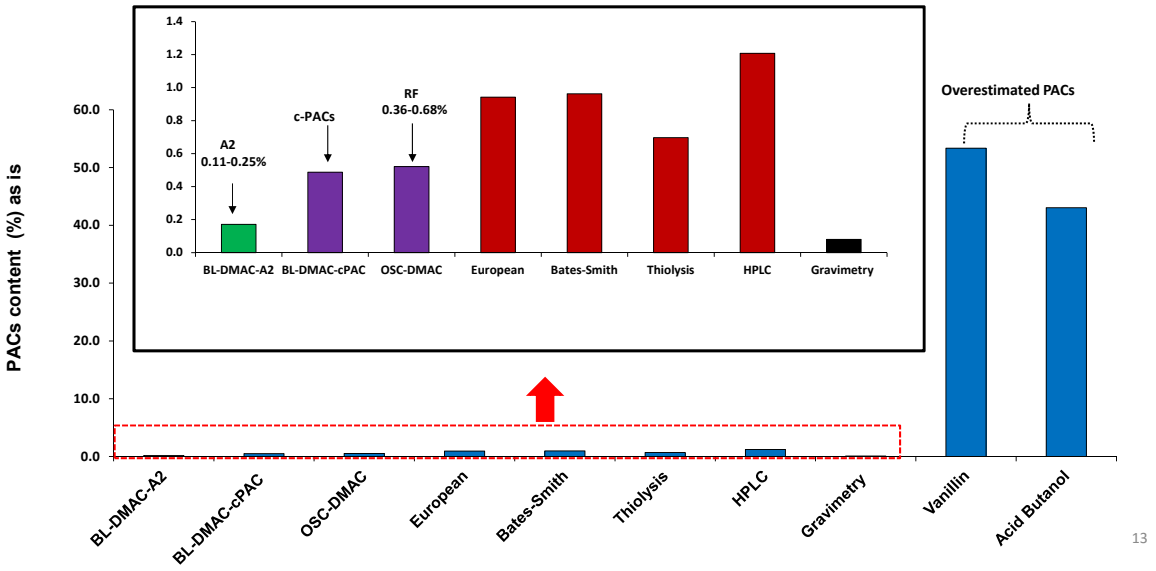
Existing Methods (General)

- Gravimetric assays
  - Bioassay directed fractionation
  - Ytterbium precipitate
- DMAC based colorimetric assays
  - BL-DMAC
  - ICT BL-DMAC
  - CPS BL-DMAC
  - OSC DMAC
- Vanillin colorimetric assay
- Acid Butanol colorimetric assay
- Bates-Smith colorimetric assay
- Thiolysis/Phloroglucinolysis
- Chromatography
  - HPLC
  - Size exclusion

PAC Method Survey Study

Method	Principal	Standard	Blank	Pros vs. Cons
BL-DMAC	DMAC react with terminal unit of PAC molecules to form a colored compound detected at 640 nm	A2	solvent	Fast, high throughput; standard no ideal
ICT BL-DMAC		A2	solvent	
CPS BL-DMAC		A2	solvent	
CPS DMAC-c PAC		c-PACs	solvent	c-PAC is more accurate than A2; not commercially available
OSC-DMAC		RF	solvent	Good for cranberry products; not accepted outside OSC
Vanillin	Vanillin react with PAC to form a colored compound detected at 500 nm	catechin	sample	Time consuming; less sensitive; overestimated PACs
Acid Butanol	PACs molecules are cleaved and converted to anthocyanidins detected at 550 nm	c-PACs	solvent	Easy to operate; overestimate PACs; water content and ions affect results
Bates-Smith			sample	Easy to operate; Water content and metal ions affect results; side reaction
European Pharmacopoeia		RF	solvent	A pharmacopeia method; for hawthorn berries
Thiolysis	Degradation of PACs into monomers and then analysed using HPLC	epicatechin	solvent	Total PACs and mean DP; Thiol agent is not lab-friendly; time consuming
HPLC	2-8 mers are separated and quantified, polymers>10 are eluted together	epicatechin A2, RF	solvent	USDA accepted method; No response factor for A-type oligomers
Gravimetry	PACs are extracted, purified and weighted	NA	NA	Time consuming, easy to overload

PACs Content in Fruit



13

Regulatory Guidance (if any)

- To date there has been only one regulation issued regarding the proanthocyanidin content of cranberry products
- In 2004 the French agency AFSSA, now known as ANSES, approved a urinary tract health claim saying a product must contain 36 mg of proanthocyanidins
- In 2010 this claim was modified to say a product must contain 36 mg of proanthocyanidins as measured by the BL-DMAC method, which had been recently published by Prior, et. al.

Proposed Fitness for Purpose

The method should be applicable to the analysis of cranberry fruit, juice, beverage, dried cranberry, cranberry sauce, ingredients (concentrates, extracts and powders) and dietary supplement formulations, applicable to two potential purposes:

1. Quantitative QC method

   Able to quantify total proanthocyanidin content, preferentially as the total sum of all individual oligomers and polymers present, or alternatively as the total sum with reference to a suitable surrogate standard, in samples typically ranging from 0.01% to 55% on a w/w basis

2. Qualitative method to verify authenticity

   Able to provide information on the distribution of proanthocyanidin oligomers and polymers present and confirm presence of A-type versus B-type

AOAC International
Stakeholder Panel on Strategic Food Analytical Methods: Emerging Contaminants & Multi-Residue Analysis of Veterinary Drugs

Lucie RACAULT, Thomas BESSAIRE, Aurélien DESMARCHELIER & Thierry DELATOUR*
Nestlé Research Centre, Lausanne, Switzerland

*Member of *Chemical Contaminants and Residues in Food* Community
*Chair of Subgroup *Environmental & Emerging Contaminants*

Sept. 18, 2016

AOAC 130th Annual Meeting & Exposition, Dallas, TX, Sept. 18-21, 2016

Community
Chemical Contaminants and Residues in Food

- **Subgroup 'Veterinary drugs'**
  Meeting on Tuesday 20 September, 11:45 am – 1:15 pm
- **Subgroup 'Metals'**
  Meeting on Tuesday 20 September, 1:30 pm – 3:00 pm
- **Subgroup 'Environmental and Emerging Contaminants'**
  Meeting on Tuesday 20 September, 4:30 pm – 6:00 pm
- **Subgroup 'Pesticides'**
  Meeting on Tuesday 20 September, 6:15 pm – 7:45 pm

Community meeting on Monday 19 September, 5:00 pm – 7:00 pm

New Topics of Interest

- **Subgroup 'Environmental and Emerging Contaminants'**
  - Validation procedure (guidelines?) for fingerprinting-based methods
  - Guidelines for untargeted analysis aimed at identifying unknowns
  - Platform for suitable information in the case of a response to crisis

New Topics of Interest

- **Subgroup 'Environmental and Emerging Contaminants'**
  - Validation procedure (guidelines?) for fingerprinting-based methods
  - Guidelines for untargeted analysis aimed at identifying unknowns
  - Platform for suitable information in the case of a response to crisis

- **Subgroup 'Veterinary drugs'**
  - International Standard for multiresidue analysis of veterinary drugs in food

Veterinary Drugs

Definition

"Any substance applied or administered to any food-producing animal, such as meat or milk producing animals, poultry, fish or bees, whether used for therapeutic, prophylactic, or diagnostic purposes, or for modification of physiological functions or behaviour."

by Codex Alimentarius

Use & Actions

- **To treat an existing illness**
- **To prevent future diseases**
- **To promote growth**

Main pharmacological actions:

- **Antibiotics** to control bacterial diseases
- **Sedative, pain killers and anti-inflammatory medicines**
- **Wormers** (anthelmintics) to control internal parasites
- **Coccidiostats** to control protozoal diseases in poultry
- **Carbamates and pyrethroids** to control external parasites
- **Dyes** (Malachite green) as fungicide, parasiticide, and disinfectant in aquaculture
- **Substances having anabolic effect** (Stilbenes, antithyroid agents, steroids, resorcylic acid lactones, beta-agonists)

Regulation & Health Issues

- **MRLs:** Maximum Residue Limits from mg/kg (ppm) to < µg/kg (ppb). A withdrawal period must be respected to avoid residues in animal tissues.
- **Prohibited substances:** These substances are not allowed to be administered to food-producing animals. E.g. Listed in Commission Regulation (EU) No 37/2010 under prohibited substances for which MRLs cannot be established (e.g. Chloramphenicol, Nitrofurans)

- Antibiotic used for treating animal diseases are also applied in human medicine
- MRLs must be respected to avoid **increasing bacterial resistance to antibiotics used in therapeutics**
- **Accute**: Allergenicity/Hypersensitivity/β-Agonist
- **Long term**: Teratogens/Cancer

Antimicrobial Resistance

World Health Organization

CRITICALLY IMPORTANT ANTIMICROBIALS

- Aminoglycosides
- Carbapenems and other penems
- Cephalosporins (3rd and 4th generation)*
- Cyclic esters
- Flouro- and other quinolones*
- Glycopeptides*
- Glycylcyclines
- Lipopeptides
- Macrolides* and ketolides
- Monobactams
- Oxazolidinones
- Penicillins (natural, aminopenicillins, and antistaphylococcal)
- Polymyxins
- Rifamycins
- Drugs used solely to treat tuberculosis or other mycobacterial diseases

* Designated by the WHO as "Highest Priority Critically Important Antimicrobials."

OIE World Organisation for Animal Health

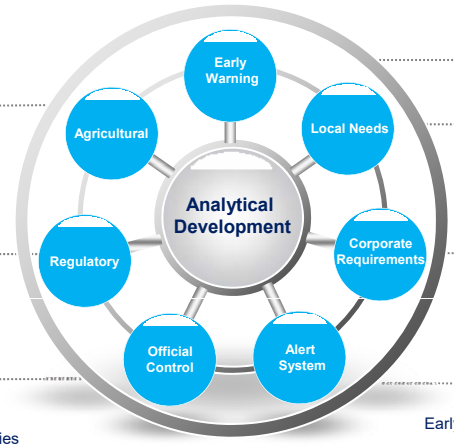
OIE LIST OF ANTIMICROBIALS OF VETERINARY IMPORTANCE

Criteria used for categorisation | List of antimicrobials

"The overlap of critical lists for human and veterinary medicine can provide further information, allowing an appropriate balance to be struck between animal health needs and public health considerations"

Integrated Approach for Analytical Development

Team of experts to define an integrated approach



Early Warning/Chemical Contaminants Experts/Corporate Quality
Assess likelihood of ocurrence
Anticipate and mitigate incidents

Agricultural Services (Corporate and Zones)
Field information
Fraud scenarios
Training

Market and specific needs
Supply constraints
Operator skills
Specific regulation
Restricted importation

Regulatory
Local regulation (e.g. EU, US, China etc…)
Codex

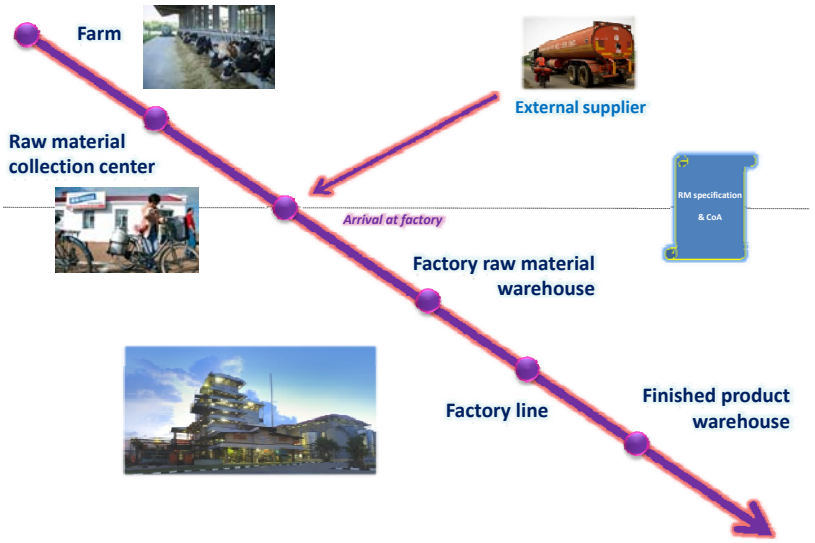
Corporate Requirements
Analytical Volume
Internal vs External Approach

Alignment on official national control plan
Alignment with authorities control plan in global monitoring program

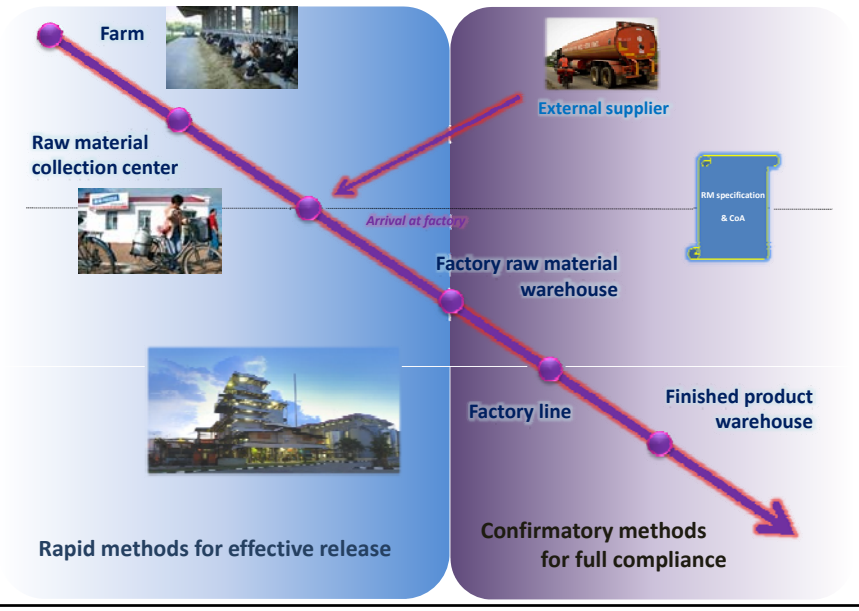
Internal Alerts System
Early Warning, Positive findings data capture system

External Alerts
Consumers, Suppliers, Contaminants network

Quality Testing along the Supply Chain & Manufacturing

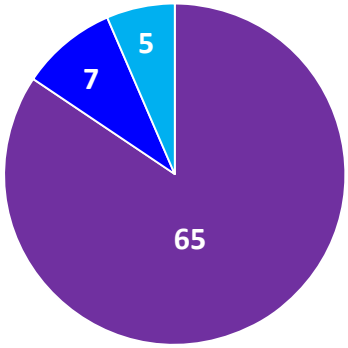


Quality Testing along the Supply Chain & Manufacturing



Literature Available for Veterinary Drugs by LC-MS/MS

Over 77 methods described from 2009 on …



… developed for a single food matrix

… developed for two food matrices

… developed for …
… more than two food matrices

https://www.scopus.com/
Keywords: Veterinary drugs, LC-MS/MS, multi-class, validation, pub year > 2009

What About Fitness-for-Purpose?

- M. Danesaki and N. Thomaidis (Analytica Chimica Acta, 2015, pp 103-121)
  - Validated level = 100 µg/kg for all the 155 compounds i.e. far above numerous MRL
  - Incomplete and/or not compliant for some Penicillins, Cephalosporins, Tetracycline, β-Agonists, Steroids …

- S. Chung and C.-H. Lam (Analytical Methods, 2015, pp 6764-6776)
  - 78 compounds without inclusion of Penicillins, Sulfonamides, or Tetracyclines
  - Incomplete and/or not compliant for some Amphenicols, Cephalosporins, Quinolones, β-Agonists, Steroids ..

- X.-J. Deng et al. (Journal of Liquid Chromatography and related Technology, 2011, pp 2286-2303)
  - 105 compounds without inclusion of Penicillins, Cephalosporins, Avermectins etc…
  - Incomplete scope for Tetracyclines

What About Fitness-for-Purpose?

- **C. Robert et al. (Food Additives and Contaminants Part A, 2013, pp 443-457)**
  - Most complete scope (154 analytes in milk, muscle, egg and honey)
  - **Incomplete and/or not compliant for some Penicillins, Cephalosporins, Tetracycline, β-Agonists, Steroids**

- **D. Chen et al. (Journal of Chromatography B, 2016, pp 82-88)**
  - Validated level claimed between for 120 compounds 1.5 – 8 µg/kg, **but validation data not shown**
  - **Calibration curve in solvent for matrices as different as edible muscles, hen eggs, and cow's milk**

- **M. Danesaki and N. Thomaidis (Analytica Chimica Acta, 2015, pp 103-121)**
  - Validated level = 100 µg/kg for all the 155 compounds i.e. **far above numerous MRL**
  - **Incomplete and/or not compliant for some Penicillins, Cephalosporins, Tetracycline, β-Agonists, Steroids …**

- **S. Chung and C.-H. Lam (Analytical Methods, 2015, pp 6764-6776)**
  - 78 compounds **without inclusion of Penicillins, Sulfonamides, or Tetracyclines**
  - **Incomplete and/or not compliant for some Amphenicols, Cephalosporins, Quinolones, β-Agonists, Steroids ..**

- **X.-J. Deng et al. (Journal of Liquid Chromatography and related Technology, 2011, pp 2286-2303)**
  - 105 compounds **without inclusion of Penicillins, Cephalosporins, Avermectins etc…**
  - **Incomplete scope for Tetracyclines**

A Compliance-driven Approach

Multi-class (*n* = 105)

Aminocoumarins (1), Amphenicols (3), Diaminopyrimidines (2), Lincosamides (2), Macrolides (8), Quinolones (18), Rifamycins (2), Streptogramins (1), Sulfonamides (22), Avermectins (6), Benzimidazoles (14), Diphenylsulfides (1), Halogenated phenols (1), Imidazothiazoles (1), Organophosphates (1), Salicylanilides (4), Tetrahydropyrimidines (1), NSAID (5), Coccidiostats (12), Tranquilizers (3).

A Compliance-driven Approach

Tetracyclines (*n* = 10)	Chlortetracycline + 4-epi, Demeclocycline + 4-epi, Doxycycline + 6-epi, Oxytetracycline + 4-epi, Tetracycline + 4-epi.
Aminoglycosides (*n* = 13)	Apramycin, Dihydrostreptomycin, Gentamycin (C1, C1a, C2), Hygromycin B, Kanamycin (A), Neomycin (B), Paromomycin, Spectinomycin, Streptomycin, Tobramycin, Amikacin.
Beta-lactams (*n* = 23)	Penicillins (12), Cephalosoprins (11).
Growth pro. (*n* = 28)	β-Agonists (8), Anabolic steroids (6), Stilbenes (3), Resorcyclic lactones (3), Corticosteroids (7).
Multi-class (*n* = 105)	Aminocoumarins (1), Amphenicols (3), Diaminopyrimidines (2), Lincosamides (2), Macrolides (8), Quinolones (18), Rifamycins (2), Streptogramins (1), Sulfonamides (22), Avermectins (6), Benzimidazoles (14), Diphenylsulfides (1), Halogenated phenols (1), Imidazothiazoles (1), Organophosphates (1), Salicylanilides (4), Tetrahydropyrimidines (1), NSAID (5), Coccidiostats (12), Tranquilizers (3).

A Compliance-driven Approach

n = 179

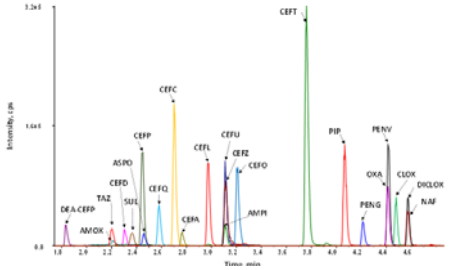
Tetracyclines (*n* = 10)	Chlortetracycline + 4-epi, Demeclocycline + 4-epi, Doxycycline + 6-epi, Oxytetracycline + 4-epi, Tetracycline + 4-epi.
Aminoglycosides (*n* = 13)	Apramycin, Dihydrostreptomycin, Gentamycin (C1, C1a, C2), Hygromycin B, Kanamycin (A), Neomycin (B), Paromomycin, Spectinomycin, Streptomycin, Tobramycin, Amikacin.
Beta-lactams (*n* = 23)	Penicillins (12), Cephalosoprins (11).
Growth pro. (*n* = 28)	β-Agonists (8), Anabolic steroids (6), Stilbenes (3), Resorcyclic lactones (3), Corticosteroids (7).
Multi-class (*n* = 105)	Aminocoumarins (1), Amphenicols (3), Diaminopyrimidines (2), Lincosamides (2), Macrolides (8), Quinolones (18), Rifamycins (2), Streptogramins (1), Sulfonamides (22), Avermectins (6), Benzimidazoles (14), Diphenylsulfides (1), Halogenated phenols (1), Imidazothiazoles (1), Organophosphates (1), Salicylanilides (4), Tetrahydropyrimidines (1), NSAID (5), Coccidiostats (12), Tranquilizers (3).

Stream for 23 β-Lactams

- **Low MRL requirement e.g. 4 µg/kg in milk for Amoxicillin** (*Commission Regulation (EU) No 37/2010*)
- **Massively used as broad spectrum antibiotic.** *No amoxicillin = no method for β-lactams*
- **Polar compound(s) with multiple pK_a but sensitive to acidic/basic conditions**

→Multiclass, Multiresidue Methods fail to cover all β-lactams at their MRL

Need a separate method … but complete and fit-for-compliance



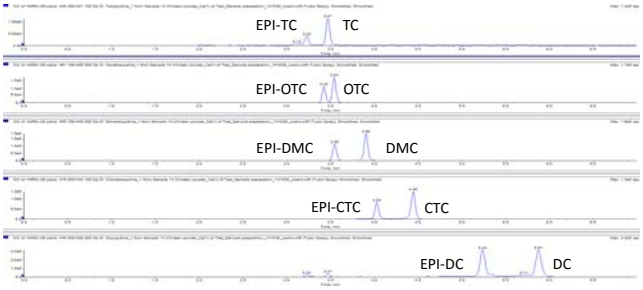
LC-MS/MS chromatograms of 23 β-lactams in an infant formula spiked at 1x STC level

Stream for 10 Tetracyclines

- **Chlortetracycline, Oxytetracycline, Tetracycline are regulated as «the sum of parent drug and its epimer»** (*Commission Regulation (EU) No 37/2010*)
- **Chromatographic challenges:**
  - Separation between parent drug and corresponding epimer
  - Chelation of compounds in the LC-MS/MS system

→Multiclass, Multiresidue Methods fail to cover all tetracyclines and epimers

Need a separate method … but complete and fit-for-compliance



LC-MS/MS chromatograms of 10 Tetracyclines in chicken powder spiked at 1x STC (25 µg/kg)

Relevant Food Commodities

An approach including raw materials, semi-finished and finished products

Milk-based products	Meat/Seafood-based products
	

The «USUALLY-SHOWN» matrices

- Raw milk
- Fresh or cooked meat, fish and seafood

Relevant Food Commodities

An approach including raw materials, semi-finished and finished products

Milk-based products	Meat/Seafood-based products
	

The «USUALLY-SHOWN» matrices

- Raw milk
- Fresh or cooked meat, fish and seafood

The «FORGOTTEN» matrices

- Milk fractions
  (e.g. Skimmed milk powder, whey protein concentrate/hydrolysate, lactose etc...)
- Formulae with milk
  (e.g. Infant, follow-on, grow-up formulae; hydrolysed formulae; adult formulae etc...)
- Infant Cereals with milk
- Meat, fish and seafood powder
  (e.g. Shrimp, duck, meat, pork, lamb, beef, chicken, veal etc...)
- Infant Cereals with meat tissues
- Babyfood in jars and pots
  (based on vegetables, meat/fish, pasta, cereals, vegetable oil etc..)

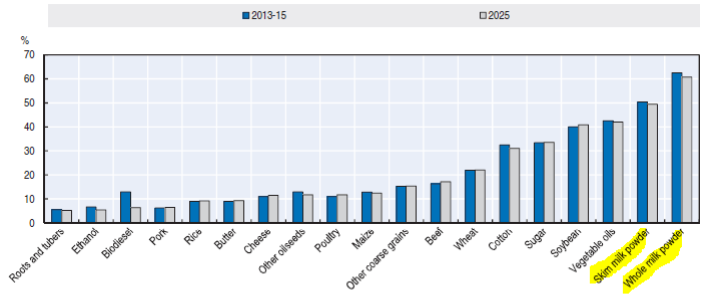
✓ Need for «Quick Easy Cheap Rugged and Safe» like methods

Beyond Raw Milk Analysis

"Whole milk powder and skimmed milk powder will remain the most traded agricultural commodities"

Figure 1.10. **Share of production traded**

Share of exports in total production



Source: OECD/FAO (2016), "OECD-FAO Agricultural Outlook", OECD *Agriculture statistics* (database), *http://dx.doi.org/10.1787/agr-data-en.*

StatLink http://dx.doi.org/10.1787/888933381249

***Additionnal consideration:* Drugs are transferred from whole milk to milk fractions during processing**

Hakk et al., J. Agric Food Chem, 2016, 64, 326-335

Monitoring Data for Veterinary Drug Residues

MILK DRUG RESIDUE SAMPLING SURVEY

FDA

Food and Drug Administration
Department of Health and Human Services

March 2015

A total of **fifteen** confirmed positive milk samples were identified **out of the 1'912** total samples.

0.78%

TECHNICAL REPORT

efsa

Report for 2014 on the results from the monitoring of veterinary medicinal product residues and other substances in live animals and animal products

European Food Safety Authority

In 2012, there were just over **1'000** non-compliant samples from over **425'000** total samples.

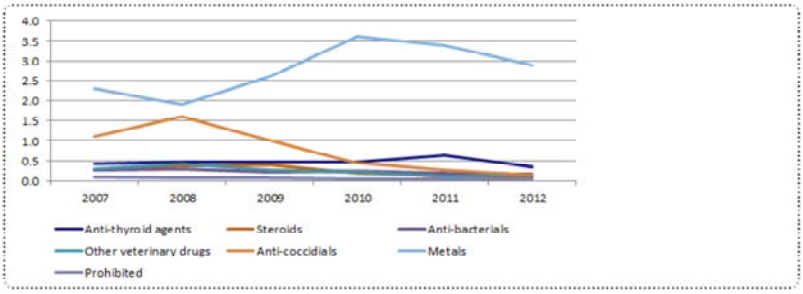
0.24%

Monitoring Data for Veterinary Drug Residues

Across the EU monitoring of the levels of these residues in food-producing animals and animal-derived foods takes place annually. The substances can be grouped into six broad categories: hormones, beta-antagonists, prohibited substances, antibacterials, other veterinary drugs, and other substances/environmental contaminants. The animals and foods monitored are bovines, pigs, sheep and goats, horses, poultry, rabbit, farmed game, wild game, aquaculture, milk, eggs and honey.

Overall, non-compliance is steady or decreasing

Percentage of non-compliant samples and in selected categories 2007-2012



Analytical Strategy

- **Aim** is to check if samples are below or potentially above the Screening Target Concentration (STC)
- **Results** are either *< STC* (given in µg/kg) or *Suspect*
- **Response** = relative comparison between Peak Area in Unspiked Sample (A_{us}) vs. Peak Area in the related Spiked Sample (A_s)

Validation scheme according to EU CRL 2010 / 01 / 20

Samples

Milk-based products
Milk fractions (16), infant formulae & milk powders (15), milk-based infant cereals (5)

Meat/Seafood products
Meat/seafood powders (10), Meat /seafood fresh and cooked (10), meat-based baby-foods

Design

67 samples

Fortified at 0, 1, 2 STC

Three analysts involved

Over 15 days

Quality Criteria

Cut-off level

False suspect rate: < 10%

False negative rate: < 5%

Retention time: < 0.2 min

Identification: 2 MRM

Full validation by the developing lab + Multi-site implementation (France, Singapore, USA)

Take-Home Message

- Uncontrolled occurrence of veterinary drugs in food is a health concern, particularly with regard to antimicrobial resistance.
- Multiresidue analysis is needed for an effective control.
- Mass spectrometry is needed for full compliance testing.
- A single LC-MS-based method capable to demonstrate full compliance of veterinary drugs in food does not exist so far.
- Matrix scope should represent current practices in terms of trade and business.
- Method performance should fit with throughput and postive rate for a *as-low-cost-as-possible* analysis.

SPSFAM – SEPTEMBER 19, 2016

STAKEHOLDER PANEL ON STRATEGIC FOOD ANALYTICAL METHODS

DALLAS, TEXAS, USA

RESOURCES

Key Staff Contacts:

Name	Role	Email	Telephone
Scott Coates	AOAC Chief Scientific Officer	scoates@aoac.org	301.924.7077 x 137
Christopher Dent	Standards Development Coordinator	cdent@aoac.org	301.924.7077 x 119
Dawn Frazier	Executive, Scientific Business Development	dfrazier@aoac.org	301.924.7077 x 117
Deborah McKenzie	Sr. Director, Standards Development and Method Approval Processes	dmckenzie@aoac.org	301.924.7077 x 157

Useful Web Links:

AOAC Website: http://www.aoac.org

SPSFAM Microsite: http://bit.ly/1GkSJ07

Working Group Sign Up Form: https://form.jotform.com/52325189177158

LOOK OUT FOR INVITATIONS TO THE 2016 AOAC MID-YEAR MEETING IN MARYLAND, SCHEDULED FOR

MARCH 13 – MARCH 17, 2017!

VOLUNTEER OPPORTUNITIES

Volunteers of AOAC INTERNATIONAL are essential to the fulfillment of our mission of serving the communities of analytical science by developing voluntary consensus standards and providing fit for purpose methods and services for assuring quality measurements. To learn how to become more involved, please contact the liaison for each group or the AOAC INTERNATIONAL Membership Department and/or visit the AOAC website for calls for experts or nominations.

AOAC BOARD OF DIRECTORS and SUPPORTING VOLUNTEER BOARDS & COMMITTEES

AOAC INTERNATIONAL Board of Directors
Mission: To establish policies and manage the affairs of the Association between meetings of the Membership
Liaison: E. James Bradford, jbradford@aoac.org

Official Methods Board
Mission: To serve the Association in a scientific and advisory capacity on methods and the process of their adoption. The OMB shall be responsible for implementation of procedures adopted by the Board of Directors.
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
Delia Boyd, dboyd@aoac.org

Committee on Membership
Mission: To recommend policies and procedures for all types of AOAC memberships.
Liaisons: Jonathan Goodwin, jgoodwin@aoac.org
May R.Jones, mjones@aoac.org

Tellers Committee
Mission: To audit and certify the results of the AOAC INTERNATIONAL mail ballots.
Liaison: Alicia Meiklejohn, ameiklejohn@aoac.org

Harvey W. Wiley Award Committee
Mission: To select the recipient of the annual AOAC INTERNATIONAL Harvey W. Wiley Award.
Liaison: May R. Jones, mjones@aoac.org

Technical Programming Council
Mission: To provide advice and support in the development and oversight of AOAC's professional development programs.
Liaison: Lauren Chelf, lchelf@aoac.org

Editorial Board
Mission: To oversee the development, editing, and publishing of all Association publications, to provide for long and short range publication planning.
Liaison: Robert Rathbone, rrathbone@aoac.org

Laboratory Proficiency Testing Program Advisory Committee
Mission: To serve the Association in a scientific and advisory capacity in the operation of the AOAC Laboratory Proficiency Testing Program and related activities.
Liaison: Arlene Fox, afox@aoac.org

Committee on Fellows
Mission: To select and recommend to the AOAC Board of Directors candidates for the Fellow of AOAC INTERNATIONAL award.
Liaison: May R. Jones, mjones@aoac.org

Committee on Sections
Mission: To foster communication between AOAC Sections and to provide and make recommendations to the Association on policies and procedures pertaining to AOAC Sections.
Liaisons: May R. Jones, sections@aoac.org;
Jonathan Goodwin, sections@aoac.org;

VOLUNTARY CONSENSUS STANDARDS STAKEHOLDER PANELS & WORKING GROUPS

Please contact the liaisons and standards coordinators for the stakeholder panels to get involved.

International Stakeholder Panel on Alternative Methods (ISPAM)
ISPAM Chair: Erin Crowley, Q Laboratories
Liaison: Krystyna McIver, kmciver@aoac.org
Standards Development Program Manager: Delia Boyd, dboyd@aoac.org

Stakeholder Panel on Agent Detection Assays (SPADA)
Chair: Matthew Davenport, Johns Hopkins University, APL
Liaison: Krystyna McIver, kmciver@aoac.org
Standards Development Coordinator: Christopher Dent, cdent@aoac.org

Stakeholder Panel on Infant Formula and Adult Nutritionals (SPIFAN)
Chair: Darryl Sullivan, Covance Laboratories
Liaison: Alicia Meiklejohn, ameiklejohn@aoac.org
Standards Development Program Manager: Delia Boyd, dboyd@aoac.org

Stakeholder Panel on Dietary Supplements (SPDS)
Chair: Darryl Sullivan, Covance Laboratories
Liaison: Dawn Frazier, dfrazier@aoac.org
Standards Development Coordinator: Christopher Dent, cdent@aoac.org

Stakeholder Panel on Strategic Food Analytical Methods (SPSFAM)
Chair: Erik Konings, Nestle Research Center
Liaison: Dawn Frazier, dfrazier@aoac.org
Standards Development Coordinator: Christopher Dent, cdent@aoac.org

Stakeholder Panel Working Groups Being Launched and Forming

SPDS Working Group on Free Amino Acids
SPDS Working Group on Ginger
SPDS Working Group on Vitamin K
SPSFAM Working Group on Cannabis Potency
SPSFAM Working Group on Proanthocyanidins in Cranberry Products
ISPAM Working Group on Food Allergen Assays

Please contact liaisons for ongoing activities for these groups.

Updated 9-6-2016

ACTIVE METHOD EXPERT REVIEW PANELS (ERPs) & ADVISORY COMMITTEES

Please contact the liaison for more information on volunteer openings in the following panels or advisory committees.

AOAC Committee on Safety
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
Delia Boyd, dboyd@aoac.org

AOAC ERP for SPIFAN Nutrient Methods
Liaisons: Alicia Meiklejohn, ameiklejohn@aoac.org
Delia Boyd, dboyd@aoac.org

AOAC ERP for Veterinary Drug Residues
Liaisons: Dawn Frazier, dfrazier@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for SPSFAM Flavanol Methods
Liaisons: Dawn Frazier, dfrazier@aoac.org
Christopher Dent, cdent@aoac.org

AOAC ERP for Proprietary Vitamin Methods (RI)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for Gluten Assays (RI)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for Fertilizer Methods (RI)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for PAH Methods (RI)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for SPIFAN Pesticide Contaminant Methods
Liaisons: Alicia Meiklejohn, ameiklejohn@aoac.org
Delia Boyd, dboyd@aoac.org

AOAC ERPs for SPDS Methods – Ashwaghanda, Folin C, and *Mitrogyna speciosa*
Liaisons: Dawn Frazier, dfrazier@aoac.org
Christopher Dent, cdent@aoac.org

AOAC ERP for Solids in Syrups-Method Modification of AOAC 932.14 (RI)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for SPSFAM Select Food Allergen Methods
Liaisons: Dawn Frazier, dfrazier@aoac.org
Christopher Dent, cdent@aoac.org

AOAC Committee on Statistics
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
Delia Boyd, dboyd@aoac.org

AOAC ERP for SPIFAN Whey Protein:Casein Methods
Liaisons: Alicia Meiklejohn, ameiklejohn@aoac.org
Delia Boyd, dboyd@aoac.org

AOAC ERP for SPSFAM Antioxidant Methods
Liaisons: Dawn Frazier, dfrazier@aoac.org
Christopher Dent, cdent@aoac.org

AOAC ERP for SPSFAM Heavy Metal Methods
Liaisons: Dawn Frazier, dfrazier@aoac.org
Christopher Dent, cdent@aoac.org

AOAC ERP for Microbiology Methods for Food and Environmental Surfaces (RI)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for Milk Protein Methods (RI) (FORMING)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for Dietary Starches in Feeds Methods (RI)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERP for Pesticide Residues in Tea Methods (RI)
Liaisons: Deborah McKenzie, dmckenzie@aoac.org
La'Kia Phillips, lphillips@aoac.org

AOAC ERPs for SPDS Methods – Anthocyanins, Chondrotin, and PDE5 Inhibitors
Liaisons: Dawn Frazier, dfrazier@aoac.org
Christopher Dent, cdent@aoac.org

AOAC ERPs for SPDS Methods – Aloin, Cinnamon, and Tea
Liaisons: Dawn Frazier, dfrazier@aoac.org
Christopher Dent, cdent@aoac.org

AOAC ERP for SPSFAM Ethanol in Kombucha (Tea) Methods
Liaisons: Dawn Frazier, dfrazier@aoac.org
Christopher Dent, cdent@aoac.org

AOAC Experts: *Formerly known as General Referees and Process Experts are subject matter experts who may serve **AOAC® in** an advisory capacity.*
Method Authors: *Formerly known as Study Directors are individuals or scientists who choose, adapt, or develop a method; subject it to the appropriate evaluation; and submit it to the AOAC review process and follow it through with the ERP.*

COMMUNITIES & COMMUNITY-BASED TASK FORCES

Agricultural Materials Community
Chair: Bill Hall, Bill.Hall@mosaicco.com
Chemical Contaminants & Residues in Foods Community
Co-Chair: Steven Lehotay, steven.lehotay@ars.usda.gov
Co-chair: Kate Mastovska, Katerina.Mastovska@covance.com
Task Force on Marine and Freshwater Toxins
Co-Chair: Jim Hungerford, james.hungerford@fda.hhs.gov
Co-chair: Ana Gago-Martinez, anagago@uvigo.es
Mycotoxins Community
Chair: Joerg Stroka, Joerg.STROKA@ec.europa.eu
Food Allergens Community
Co-Chair: Jupiter Yeung, Jupiter.Yeung@rd.nestle.com
Co-chair: Carmen Diaz, carmen.diaz.amigo@gmail.com
Water and Wastewater Community
Chair: Ed Askew, efaskew@hotmail.com
Technical Committee on Juice and Juice Products
Chair: Ramin Jahromi, RaminJahromi@eurofinsus.com

For openings on the ERPs and Advisory Committees, AOAC issues Calls for Experts.
Please contact the liaison for more information on potential volunteer openings.

Updated 9-6-2016

SPSFAM Roster and Mailing List

Not on this list? Let us know! Email SPSFAM@aoac.org.

Position	Full Name	Organization
Chair	Erik J. M. Konings	Nestle Research Center
Member	Vanessa Abercrombie	Agilent Technologies, Inc.
Member	David James Almy, M.S.	Neogen Corporation
Member	W. Bradley Barrett	GERSTEL, Inc.
Member	Michael Beshore	Humm Kombucha LLC
Member	Tim Beshore	Chemours
Member	Sneh D. Bhandari, Ph.D	Merieux NutriSciences
Member	Joe Boison, Ph.D	Canadian Food Inspection Agency
Member	Michelle Briscoe	Brooks Applied Labs
Member	Jeannie Buscher	Buchi Kombucha
Member	Jim Cali	Promega Corporation
Member	Esther Campos-Gimenez	Nestle Research Center
Member	Evan Chaney	
Member	Mr. Niladri Sekhar Chatterjee, Ph.D	Indian Agricultural Research Institute
Member	Mike Clark	Bio-Rad Laboratories
Member	Robert Clifford, Ph.D.	Shimadzu Scientific Instruments, Inc.
Member	Geoffrey Cottenet	Nestle Research Center
Member	Tim Croley, Ph.D	US FDA - CFSAN
Member	Erin Sutphin Crowley	Q Laboratories, Inc.
Member	Hannah Crum	Kombucha Brewers International
Member	David Cunningham	Ocean Spray Cranberries, Inc.
Member	GT Dave	Millennium Products, Inc.
Member	Jonathan W. DeVries, Sr.	Retired
Member	Carmen Diaz-Amigo	
Member	Robert Donofrio	Neogen Corporation
Member	Blake E. Ebersole	Verdure Sciences
Member	Stefan Ehling	Abbott Nutrition
Member	Katherine Fiedler	U.S. FDA
Member	Jodie Fung	Kombucha Brewers International
Member	Andrew Fussell	PANalytical
Member	Eric A.E. Garber, Ph.D	US FDA
Member	Russell Gerads	Brooks Rand Labs, LLC
Member	Brendon D. Gill	Fonterra Co-operative Group Ltd.
Member	Ms. Qian F. Graves	FDA - CFSAN
Member	Jasmine Hagan, B.S.	ELISA Technologies, Inc.
Member	Cathy A. Halverson	TTB
Member	Nicole Hart	Agilent Technologies
Member	Kevin Hegarty	Effendorf
Member	Norma R. Hill	US Treasury (Retired)
Member	Gregory L. Hostetler	Perrigo / PBM Nutritionals
Member	Min Huang	Frontage Laboratories, Inc.

SPSFAM Roster and Mailing List

Not on this list? Let us know! Email SPSFAM@aoac.org.

Member	Prashant Ingle	
Member	Brian P. Jackson	Dartmouth College
Member	Greg Jaudzems	Nestle USA, Inc
Member	Rasu Jayabalan	National Institute Of Technology Rourkela
Member	George Joseph, Ph.D	AsureQuality, New Zealand
Member	David C. Kennedy, Ph.D	Phenomenex
Member	Barbro Inga Kristina Kollander, Ph.D	National Food Agency
Member	Kevin Kubachka	US FDA
Member	Markus Lacorn	R-Biopharm AG
Member	Alex LaGory	Kombucha Brewers International
Member	John Lawry	Covance
Member	Mr. John W. Lee	MasterFoods USA
Member	Soo-Kwang Lee	FDA
Member	Qi Lin, Ph.D	Abbott Nutrition R&D
Member	Daniel Lopez-ferrer	Thermo Scientific
Member	Farzaneh Maniei, MS	The Coca-Cola Company
Member	Vicky Manti	Friesland Campina Domo
Member	Eric Marceau	Canadian Food Inspection Agency (CFIA)
Member	Elaine Catherine Marley, Ph.D	R-Biopharm Rhone Ltd
Member	Katerina Mastovska, Ph.D	Covance Laboratories
Member	Mary T. McBride, Ph.D.	Agilent Technologies, Inc.
Member	Paul Milne	Keurig Green Mountain, Inc.
Member	William Mindak	FDA/CFSAN
Member	Dr. Armen Mirzoian	Alcohol And Tobacco Tax And Trade Bureau
Member	Allen Misa	Phenomenex, Inc.
Member	Deepali Mohindra	Thermo Fisher Scientific
Member	Lisa Monteroso	3M Food Safety
Member	Cory J Murphy	Canadian Food Inspection Agency
Member	Maria Ofitserova	Pickering Laboratories, Inc.
Member	Vincent Paez	SCIEX
Member	Christine Parker	FDA
Member	Son Quang Pham, Ph.D	Abbott
Member	Theresa Pham	Holy Kombucha, Inc.
Member	Melissa Meaney Phillips	NIST
Member	Tom Phillips	MD Department Of Agriculture
Member	Tom Phillips	MD Department Of Agriculture
Member	Tom Phillips	MD Department Of Agriculture
Member	Eric Poitevin	Nestle Research Center
Member	Bert Popping, Ph.D	Mérieux NutriSciences
Member	Rick Reba	Nestle USA, Inc.
Member	Catherine A. Rimmer	NIST
Member	Shauna F. Roman	RB (Reckitt Benckiser)

SPSFAM Roster and Mailing List

Not on this list? Let us know! Email SPSFAM@aoac.org.

Member	Joe Romano	Waters Corporation
Member	Louis M. Salvati, M.S.	Abbott Laboratories
Member	Andre Schreiber	SCIEX
Member	Brooke Schwartz	Brooke Schwartz Consulting
Member	Jenny Scifres	USDA FSIS OPHS LQAD ALP
Member	Jennifer Sealey-Voyksner, Ph.D	ImmunogenX
Member	Christopher Smith	The Coca-Cola Company
Member	Katherine Stenerson	MilliporeSigma
Member	Cheryl Stephenson, Ph.D.	Eurofins Central Analytical Laboratory
Member	Joan Stevens	Agilent Technologies
Member	Rachel Stryffeler	Coca-Cola Company
Member	Mr. Darryl M. Sullivan	Covance Laboratories
Member	Julie Sundgaard	ROMER Labs Inc
Member	John Szpylka	Mérieux NutriSciences
Member	Steve Tennyson	Perrigo Nutritionals
Member	Daina Trout	Health-Ade LLC
Member	Justin Trout	Health-Ade Kombucha
Member	Socrates Trujillo, Ph.D	US FDA
Member	Jolanta Vidugiriene	Promega
Member	Azza M. Wagdy	Edgar A. Weber & Co.
Member	Sue (Shuimei) Wang, Ph.D	ITRI
Member	Wayne Wargo	Abbott Nutrition
Member	Guy Weerasekera	Mead Johnson Nutrition
Member	Laura Wood	NIST
Member	Xianli Wu	Beltsville Human Nutrition Research Center, USDA-ARS
Member	Chen Zhang	Coca-Cola Company
Member	Yao Zhou	Shanghai Entry Exit Inspection And Quarantine Bureau
Member	Patrick Martin Zoder, MS	PALL Corporation
Member	Jerry Zweigenbaum	Agilent Technologies, Inc.
AOAC Staff	Scott G. Coates	AOAC INTERNATIONAL
AOAC Staff	Christopher Dent	AOAC INTERNATIONAL
AOAC Staff	Dawn L. Frazier	AOAC INTERNATIONAL
AOAC Staff	Deborah McKenzie	AOAC INTERNATIONAL

AOAC Stakeholder Panel Voting Members

AOAC INTERNATIONAL (AOAC) assembles stakeholder panels to develop voluntary consensus standards. While AOAC maintains transparency and openness in accordance with national and international guidance and regulations for standards development and its policies and procedures for assembling stakeholder panels, its policies and procedures also ensures that there is a balance of interests and perspectives in achieving consensus of the stakeholder panel.

Due Process and Balance

All AOAC stakeholder panels are diverse and can vary in size. Where a stakeholder panel is not balanced or if it is significantly large whereby consensus of the general assembly may be impractical, a balanced representative voting panel will be used to demonstrate consensus. AOAC encourages ALL stakeholders to participate in deliberations during stakeholder panel meetings and working group meetings, in addition to participating during any posted comment periods. To ensure that there is a balance of interests and perspectives, a ***representative subset*** of the stakeholder panel, the voting members, is selected to reach consensus for the development of AOAC voluntary consensus standards.

Composition

Voting members represent the perspectives of the larger stakeholder panel. The voting members consist of no more than ¼ to 1/3 of the total number of stakeholders in registered. Primary and secondary representative voting members are approved. Every attempt is made to approve a panel of voting members that represents all perspectives of the stakeholder panel. In the event of a primary voting member is not able to attend, and no alternate has been approved, the stakeholder panel chair, working with AOAC can provisionally approve an alternate from those in attendance to assure balance and lack of dominance. For stakeholder panels with scopes including diverse topics, the voting member representatives may be rotated to include other stakeholders for successive meetings to ensure a lack of dominance by any particular stakeholder.

Approval Process

AOAC works with the chair of the stakeholder panel and potentially other key stakeholders to develop a proposed representative voting member panel. Following AOAC policies and procedures, the proposed voting members and documentation are submitted to the AOAC Official Methods Board (OMB) for review and approval. The OMB's review ensures that the proposed panel is balanced in interests and perspectives representing the stakeholder panel and a lack of dominance.

Roles and Responsibilities

Every stakeholder has a voice and every stakeholder is entitled to state his/her or organizational perspective(s). This is due process. In developing AOAC standards, stakeholder consensus is demonstrated by 2/3 vote (67%) in favor of a motion to adopt a standard. It is important to note: Individual voting members do not have any additional weight, voice or status in stakeholder deliberations than other stakeholders. The role of the voting members is to demonstrate the consensus of the stakeholder panel. Voting members may vote in favor or against any motion and/or they may abstain. Stakeholder panel chair will moderate voting process. AOAC carefully documents the vote. It is important for voting members to be in the room during the time for voting. It is also important for voting members to inform the chair of his/her inability to serve as a voting member.

AOAC INTERNATIONAL

STAKEHOLDER PANEL ON DIETARY SUPPLEMENTS (SPDS)
WORKING GROUP CHAIR & MEMBERS

VOLUNTEER ROLE DESCRIPTION

POSITION TITLE: **Working Group Chair and Members, AOAC SPDS Working Group**
POSITION CLASSIFICATION: **Volunteer**
REPORTS TO: **SPDS Chair**
DATE PREPARED: **March 13, 2014**

POSITION SUMMARY:
In keeping with the mission of AOAC INTERNATIONAL and the goals of the Stakeholder Panel on Dietary Supplements (SPDS), working group chairs will lead their working group in the development of standards (or other tasks as assigned by the SPDS chair) for specific priority ingredients as defined by the SPDS Advisory Panel. Working group chair(s) will work with AOAC staff and stakeholders to meet the working group's goals and disseminate recommendations to the stakeholder panel and community at-large. The working group may hold meetings in person and/or via teleconference (web and video) to complete its work. The chair of the working group will moderate the working group discussions, assist in scheduling the meetings, and report the working group's recommendation back to SPDS. Working group chairs will work with AOAC to formulate the working group's recommendations into motions for SPDS's consideration.

ELIGIBILITY CRITERIA FOR SPDS WORKING GROUP CHAIR:
- Must be a key expert and/or thought leader in dietary supplements and the technologies used for priority ingredients as assigned for the specific working group.
- Must have the recommendation of the SPDS Chair.

WORKING GROUP CHAIR RESPONSIBILITIES:
- Chair meetings of the working group, moderate discussions of the working group and work with AOAC staff to facilitate working group's work.
- Work with AOAC staff and SPDS chair to identify working group members, any additional expertise/resources needed facilitate the work of the working group.
- Work as a team member and also independently.
- Present an overview on the specified priority ingredient under consideration including, but not limited to, regulatory implications, and public health and public safety challenges with methodology.
- Prepare a draft fitness for purpose statement for specified priority ingredient and technology to present to SPDS for consideration.
- Work with AOAC staff to reconcile actions and outcomes of working group deliberations.
- Using AOAC guidance to reconcile comments and address questions on SMPR.
- Present working group recommended SMPR to SPDS for review and approval.
- Work with AOAC staff and stakeholders to draft and review relevant methodology and working group documentation.
- Draft SMPR white paper for publication.
- Perform duties and reviews in timely fashion.
- Other tasks as agreed upon by working group chair, SPDS chair and AOAC staff.

DUTIES AND RESPONSIBILITIES OF THE SPDS WORKING GROUP MEMBERS:
The working group will meet either in person and via teleconference, web conferencing or by other means of communication. All communication and meetings of the working group must be facilitated through AOAC

staff. The working group's tasks will include developing standard method performance requirements (SMPRs), review of methodology, identifying expertise and other as may be requested by the SPDS chair. Working groups are not required to vote, but to show general consensus for its recommendations. The groups should meet to discuss their objectives and complete their assigned tasks. Individuals on the working groups may be tasked with their own action items and responsibilities. More than one meeting and one round of communication may be required to complete the working group's tasks. All working group participants are expected to contribute and are expected to have completed the SMPR Education Session. AOAC staff will document all working group decisions and actions.

AOAC RESOURCES:

- Referencing AOAC guidance documentation to assist in drafting the fitness for purpose statement, standard method performance requirements (SMPR), and additional work as tasked.
    1) AOAC Fitness for Purpose Statement Guideline
    2) Appendix F: Guidelines for Standard Method Performance Requirements
    3) Appendix K: Guidelines for Dietary Supplements and Botanicals

STAFF LIASON:

AOAC will assign staff to facilitate the work of the working group.

TERMS OF REVIEW:

This document will be reviewed biannually by the SPDS Chair and AOAC staff.

DATES REVISED:

Stakeholder Panel

Voting Panel – A vetted, representative, and balanced subset of the assembled stakeholders. Ideally the number of voters represents $^1/_4$ to $^1/_3$ of the assembly.

Voting Guidelines – A. motions to create a consensus based standard (ex: voting on fitness for purpose statements or Standard Method Performance Requirements) require a 2/3 vote for the motion to carry.
B. Any other motion (ex: votes to clarify information for working groups, set priorities or direction, etc.) requires a majority vote to carry.

Expert Review Panel

Voting Panel – 7 – 10 vetted experts
Quorum - The presence of **7** members or **2/3** of total vetted ERP membership, whichever is greater.
Voting Guidelines – Motions to adopt a *First Action Official Method℠ of Analysis* carry by unanimous vote on first ballot. If not unanimous, negative votes must delineate scientific reasons, and can be overridden by 2/3 of voting ERP members after due consideration. Dissenting opinions are recorded.

Working Group

Voting Panel – There is no formal voting panel. Any interested and knowledgeable party may participate. Working groups sole purpose is to provide recommendations to stakeholder panels.

Voting Guidelines –majority vote carries all motions, dissenting opinions considered by assembly and recorded.

Helpful Definitions & Terminology

Quorum	The number of members who must be present in order to validly transact business. It is determined by the number of members present, not the number present and voting. (*Fundamentals of Parliamentary Law and Procedure, 3rd edition. p. 151*).
Representative Voting Panel Members	Every member has an obligation to vote and the right to abstain.
Abstentions	Abstentions reduce the number required to obtain a majority of those present and voting. They are only counted to confirm the presence of a quorum. (*Fundamentals of Parliamentary Law and Procedure, 3rd edition. p. 237).*
Order	Meetings should address only one item of business at one time (only one pending motion at a time). Chairs should not permit digression or introduction of different topics until the business at hand is resolved. No pending motions while changing topics. (*Fundamentals of Parliamentary Law and Procedure, 3rd edition. p. 1).* All business must be conducted with order and should be done fairly and impartially. The presiding officer should impartially ensure that each member has an opportunity to speak. *(Fundamentals of Parliamentary Law and Procedure, 3rd edition. pp. 1-2).*
Equality	All members have equal opportunity to propose motions, to participate in debate, to vote, to serve on committees or as an officer, to share in activities according to the member's abilities. *(Fundamentals of Parliamentary Law and Procedure, 3rd edition. p. 2).*
Justice	All members have the right to ask questions, to be informed, to have complex motions explained by the chair. *(Fundamentals of Parliamentary Law and Procedure, 3rd edition. p. 2).*
Minority Rights	Dissenting members have equal rights to voice opposing or minority opinions and strive to become the majority. *(Fundamentals of Parliamentary Law and Procedure, 3rd edition. p. 2).*
Majority Rights	No members, board, or officers have the right to dictate or control decisions unless the member grant such rights Members may not take any action in conflict with federal, regional or organizational laws or policies. Decisions are based on the will of the majority. *(Fundamentals of Parliamentary Law and Procedure, 3rd edition. p. 2).*

Appendix F: Guidelines for Standard Method Performance Requirements

Contents

Introduction to Standard Method Performance Requirements

Standard method performance requirements (SMPRs) are a unique and novel concept for the analytical methods community. SMPRs are voluntary consensus standards, developed by stakeholders, that prescribe the minimum analytical performance requirements for classes of analytical methods. In the past, analytical methods were evaluated and the results compared to a "gold standard" method, or if a gold standard method did not exist, then reviewers would decide retrospectively if the analytical performance was acceptable. Frequently, method developers concentrated on the process of evaluating the performance parameters of a method, and rarely set acceptance criteria. However, as the *Eurachem Guide* points out: " . . . the judgment of method suitability for its intended use is equally important . . ." (1) to the evaluation process.

International Voluntary Consensus Standards

An SMPR is a form of an international, voluntary consensus standard. A standard is an agreed, repeatable way of doing something that is published as document that contains a technical specification or other precise criteria designed to be used consistently as a rule, guideline, or definition. SMPRs are a *consensus* standards developed by stakeholders in a very controlled process that ensures that users, research organizations, government departments, and consumers work together to create a standard that meets the demands of the analytical community and technology. SMPRs are also *voluntary* standards. AOAC cannot, and does not, impose the use of SMPRs. Users are free to use SMPRs as they see fit. AOAC is very careful to include participants from as many regions of the world as possible so that SMPRs are accepted as *international* standards.

Guidance for Standard Method Performance Requirements

Commonly known as the "SMPR Guidelines." The first version of the SMPR Guidelines were drafted in 2010 in response to the increasing use and popularity of SMPRs as a vehicle to describe the analytical requirements of a method. Several early "acceptance criteria" documents were prepared for publication in late 2009, but the format of the acceptance criteria documents diverged significantly from one another in basic format. AOAC realized that a guidance document was needed to promote uniformity.

An early version of the SMPR Guidelines were used for a project to define the analytical requirements for endocrine disruptors in potable water. The guidelines proved to be extremely useful in guiding the work of the experts and resulted in uniform SMPRs. Subsequent versions of the SMPR Guidelines were used in the Stakeholder Panel for Infant Formula and Adult Nutritionals (SPIFAN) project with very positive results. The SMPR Guidelines are now published for the first time in the *Journal of AOAC INTERNATIONAL* and *Official Methods of Analysis*.

Users of the guidelines are advised that they are: (*1*) a *guidance* document, not a statute that users must conform to; and (*2*) a "living" document that is regularly updated, so users should check the AOAC website for the latest version before using these guidelines.

The SMPR Guidelines are intended to provide basic information for working groups assigned to prepare SMPRs. The guidelines consist of the standard format of an SMPR, followed by a series of informative tables and annexes.

SMPR Format

The general format for an SMPR is provided in *Annex A*.

Each SMPR is identified by a unique SMPR number consisting of the year followed by a sequential identification number (YYYY.XXX). An SMPR number is assigned when the standard is approved. By convention, the SMPR number indicates the year a standard is approved (as opposed to the year the standard is initiated). For example, SMPR 2010.003 indicates the third SMPR adopted in 2010.

The SMPR number is followed by a method name that must include the analyte(s), matrix(es), and analytical technique (unless the SMPR is truly intended to be independent of the analytical technology). The method name may also refer to a "common" name (e.g., "Kjeldahl" method).

The SMPR number and method name are followed by the name of the stakeholder panel or expert review panel that approved the SMPR, and the approval and effective dates.

Information about method requirements is itemized into nine categories: (*1*) intended use; (*2*) applicability; (*3*) analytical technique; (*4*) definitions; (*5*) method performance requirements; (*6*) system suitability; (*7*) reference materials; (*8*) validation guidance; and (*9*) maximum time-to-determination.

An SMPR for qualitative and/or identification methods may include up to three additional annexes: (*1*) inclusivity/selectivity panel; (*2*) exclusivity/cross-reactivity panel; and (*3*) environmental material panels. These annexes not required.

Informative tables.—The SMPR Guidelines contain seven informative tables that represent the distilled knowledge of many years of method evaluation, and are intended as guidance for SMPR working groups. The informative tables are not necessarily AOAC

policy. SMPR working groups are expected to apply their expertise in the development of SMPRs.

Table A1: Performance Requirements. Provides recommended performance parameters to be included into an SMPR. Table A1 is organized by five method classifications: (*1*) main component quantitative methods; (*2*) trace or contaminant quantitative methods; (*3*) main component qualitative methods; (*4*) trace or contaminant quantitative methods; and (*5*) identification methods. The table is designed to accommodate both microbiological and chemical methods. Alternate microbiological/chemical terms are provided for equivalent concepts.

Table A2: Recommended Definitions. Provides definitions for standard terms in the SMPR Guidelines. AOAC relies on *The International Vocabulary of Metrology Basic and General Concepts and Associated Terms* (VIM) and the International Organization for Standadization (ISO) for definition of terms not included in Table A2.

Table A3: Recommendations for Evaluation. Provides general guidance for evaluation of performance parameters. More detailed evaluation guidance can be found in *Appendix D, Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis* (2); *Appendix I, Guidelines for Validation of Biological Threat Agent Methods and/or Procedures* (3); *Appendix K, AOAC Guidelines for Single-Laboratory Validation of Chemical Methods for Dietary Supplements and Botanicals* (4); Codex Alimentarius Codex Procedure Manual (5); and ISO Standard 5725-1-1994 (6).

Table A4: Expected Precision (Repeatability) as a Function of Analyte Concentration. The precision of a method is the closeness of agreement between independent test results obtained under stipulated conditions. Precision is usually expressed in terms of imprecision and computed as a relative standard deviation (RSD) of the test results. The imprecision of a method increases as the concentration of the analyte decreases. This table provides target RSDs for a range of analyte concentrations.

Table A5: Expected Recovery as a Function of Analyte Concentration. Recovery is defined as the ratio of the observed mean test result to the true value. The range of the acceptable mean recovery expands as the concentration of the analyte decreases. This table provides target mean recovery ranges for analyte concentrations from 1 ppb to 100%.

Table A6: Predicted Relative Standard Deviation of Reproducibility ($PRSD_R$). This table provides the calculated $PRSD_R$ using the Horwitz formula:

$$PRSD_R = 2C^{-0.15}$$

where C is expressed as a mass fraction.

Table A7: POD and Number of Test Portions. This table provides the calculated probability of detection (POD) for given sample sizes and events (detections). A method developer can use this table to determine the number of analyses required to obtain a specific POD.

Informative annexes.—The SMPR Guidelines contain informative annexes on the topics of classification of methods, POD model, HorRat values, reference materials, and method accuracy and review. As with the informative tables, these annexes are intended to provide guidance and information to the working groups.

Initiation of an SMPR

See Figure 1 for a schematic flowchart diagram of the SMPR development process.

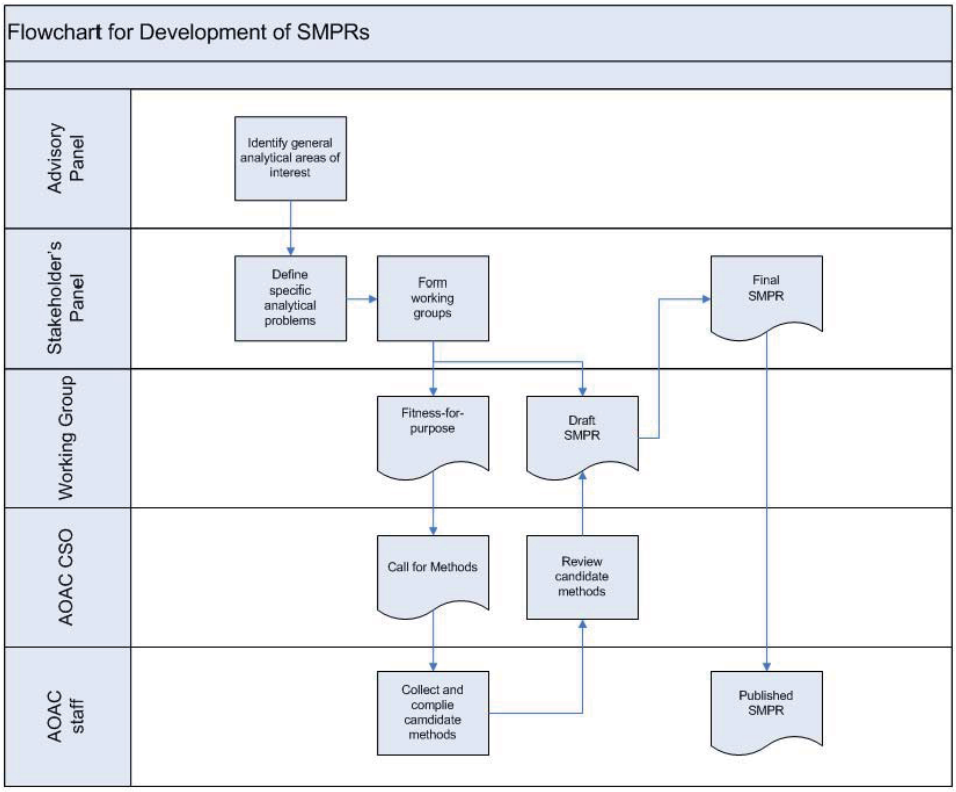


Figure 1. Schematic flowchart diagram of the SMPR development process.

Advisory panels.—Most commonly, an SMPR is created in response to an analytical need identified by an advisory panel. Advisory panels normally consist of sponsors and key stakeholders who have organized to address analytical problems. Usually, the advisory panel identifies general analytical problems, such as the need to update analytical methods for determination of nutrients in infant formula. An advisory panel, with the input of appropriate subject matter experts, also prioritizes the specific analytical problems within the general topic. This panel is critical in planning for the stakeholder panel meeting.

Stakeholder panels.—After an advisory panel has identified a general analytical problem, AOAC announces the standards development activity, identifies stakeholders, and organizes a stakeholder panel. Membership on a stakeholder panel is open to anyone materially affected by the proposed standard. AOAC recruits scientists to participate on stakeholder panels on the basis of their expertise with the analytical problem identified by the advisory panel. Experts are recruited from academia, government, nongovernmental organizations (such as ISO), industry, contract research organizations, method developers, and instrument/equipment manufacturers. AOAC employs a representative voting panel model to ensure balance with regards to stakeholder perspective, and to ensure that no particular stakeholder perspective dominates the proceedings of the stakeholder panel. All stakeholder candidates are reviewed by the AOAC Chief Scientific Officer (CSO) for relevant qualifications, and again by the Official Methods Board to ensure that the stakeholder panel is balanced and all stakeholders are fairly represented.

Stakeholder panels are extremely important as they serve several functions: (*1*) identify specific analytical topics within the general analytical problem described by the advisory panel; (*2*) form working groups to address the specific analytical topics; (*3*) identify additional subject matter experts needed for the working groups; (*4*) provide oversight of the SMPR development; and (*5*) formally adopt SMPRs originally drafted by working groups.

Working groups.—Working groups are formed by the stakeholder panel when a specific analytical topic has been identified. The primary purpose of a working group is to draft an SMPR. Working groups may also be formed to make general recommendations, such as developing a common definition to be used by multiple working groups. For example, SPIFAN formed a working group to create a definition for "infant formula" that could be shared and used by all of the SPIFAN working groups.

The process of drafting an SMPR usually requires several months, and several meetings and conference calls. An SMPR drafted by a working group is presented to a stakeholder panel. A stakeholder panel may revise, amend, or adopt a proposed SMPR on behalf of AOAC.

Fitness-for-Purpose Statement and Call for Methods

One of the first steps in organizing a project is creating a fitness-for-purpose statement. In AOAC, the fitness-for-purpose statement is a very general description of the methods needed. It is the responsibility of a working group chair to draft a fitness-for-purpose statement. A working group chair is also asked to prepare a presentation with background information about the analyte, matrix, and the nature of the analytical problem. A working group chair presents the background information and proposes a draft fitness-for-purpose statement to the presiding stakeholder panel. The stakeholder panel is asked to endorse the fitness-for-purpose statement.

The AOAC CSO prepares a call for methods based on the stakeholder panel-approved fitness-for-purpose statement. The call for methods is posted on the AOAC website and/or e-mailed to the AOAC membership and other known interested parties. AOAC staff collects and compiles candidate methods submitted in response to the call for methods. The CSO reviews and categorizes the methods.

Creating an SMPR

Starting the process of developing an SMPR can be a daunting challenge. In fact, drafting an SMPR should be a daunting challenge because the advisory panel has specifically identified an analytical problem that has yet to be resolved. Completing an SMPR can be a very rewarding experience because working group members will have worked with their colleagues through a tangle of problems and reached a consensus where before there were only questions.

It is advisable to have some representative candidate methods available for reference when a working group starts to develop an SMPR. These methods may have been submitted in response to the call for methods, or may be known to a working group member. In any case, whatever the origin of the method, candidate methods may assist working group members to determine reasonable performance requirements to be specified in the SMPR. The performance capabilities of exisiting analytical methodologies is a common question facing a working group.

Normally, a working chair and/or the AOAC CSO prepares a draft SMPR. A draft SMPR greatly facilitates the process and provides the working group with a structure from which to work.

Working group members are advised to first consider the "intended use" and "maximum time-to-determination" sections as this will greatly affect expectations for candidate methods. For example, methods intended to be used for surveillance probably need to be quick but do not require a great deal of precision, and false-positive results might be more tolerable. Whereas methods intended to be used for dispute resolution will require better accuracy, precision, and reproducibility, but time to determination is not as important.

Once a working group has agreed on the intended use of candidate methods, then it can begin to define the applicability of candidate methods. The applicability section of the SMPR is one of the most important, and sometimes most difficult, sections of the SMPR. The analyte(s) and matrixes must be explicitly identified. For chemical analytes, International Union of Pure and Applied Chemistry (IUPAC) nomenclature and/or Chemical Abstracts Service (CAS) registry numbers should be specified. Matrixes should be clearly identified including the form of the matrix such as raw, cooked, tablets, powders, etc. The nature of the matrix may affect the specific analyte. It may be advantageous to fully identify and describe the matrix before determining the specific analyte(s). It is not uncommon for working groups to revise the initial definition of the analyte(s) after the matrix(es) has been better defined.

Table 1. Example of method performance table for a single analyte

Analytical range	7.0–382.6 µg/mL	
Limit of quantitation (LOQ)	≤7.0 µg/mL	
Repeatability (RSD_r)	<10 µg/mL	≤8%
	≥10 µg/mL	≤6%

Table 2. Example of method performance table for multiple analytes

	Analyte 1		Analyte 2		Analyte 3	
Analytical range	10–20 µg/mL		100–200 µg/mL		200–500 µg/mL	
Limit of quantitation (LOQ)	≤10 µg/mL		≤100 µg/mL		≤200 µg/mL	
Repeatability (RSD_r)	<10 µg/mL	≤8%	<10 µg/mL	≤8%	<200 µg/mL	≤10%
	≥10 µg/mL	≤6%	≥10 µg/mL	≤6%	≥200 µg/mL	≤8%

For projects with multiple analytes, for example, vitamins A, D, E, and K in infant formula, it may be useful to organize a separate working group to fully describe the matrix(es) so that a common description of the matrix(es) can be applied to all of the analytes.

For single analyte SMPRs, it is most common to organize the method performance requirements into a table with 2–3 columns as illustrated in Table 1. For multiple analyte SMPRs, it is often convenient to present the requirements in an expanded table with analytes forming additional columns as illustrated in Table 2.

Once the intended use, analytical techniques, and method performance requirements have been determined, then a working group can proceed to consider the quality control parameters, such as the minimum validation requirements, system suitability procedures, and reference materials (if available). It is not uncommon that an appropriate reference material is not available. *Annex F* of the SMPR Guidelines provides comprehensive guidance for the development and use of in-house reference materials.

Most working groups are able to prepare a consensus SMPR in about 3 months.

Open Comment Period

Once a working group has produced a draft standard, AOAC opens a comment period for the standard. The comment period provides an opportunity for other stakeholders to state their perspective on the draft SMPR. All collected comments are reviewed by the AOAC CSO and the working group chair, and the comments are reconciled. If there are significant changes required to the draft standard as a result of the comments, the working group is convened to discuss and any unresolved issues will be presented for discussion at the stakeholder panel meeting.

Submission of Draft SMPRs to the Stakeholder Panel

Stakeholder panels meet several times a year at various locations. The working group chair (or designee) presents a draft SMPR to the stakeholder panel for review and discussion. A working group chair is expected to be able to explain the conclusions of the working group, discuss comments received, and to answer questions from the stakeholder panel. The members of the stakeholder panel may revise, amend, approve, or defer a decision on the proposed SMPR. A super majority of 2/3 or more of those voting is required to adopt an SMPR as an AOAC voluntary consensus standard.

Publication

Adopted SMPRs are prepared for publication by AOAC staff, and are published in the *Journal of AOAC INTERNATIONAL* and in the AOAC *Official Methods of Analysis*℠ compendium. Often, the AOAC CSO and working group chair prepare a companion article to introduce an SMPR and describe the analytical issues considered and resolved by the SMPR. An SMPR is usually published within 6 months of adoption.

Conclusion

SMPRs are a unique and novel concept for the analytical methods community. SMPRs are voluntary, consensus standards developed by stakeholders that prescribe the minimum analytical performance requirements for classes of analytical methods. The SMPR Guidelines provide a structure for working groups to use as they develop an SMPR. The guidelines have been employed in several AOAC projects and have been proven to be very useful. The guidelines are not a statute that users must conform to; they are a "living" document that is regularly updated, so users should check the AOAC website for the latest version before using the guidelines.

References

(1) Eurachem, *The Fitness for Purpose of Analytical Methods: A Laboratory Guide to Method Validation and Related Topics, Validation*, http://www.eurachem.org/guides/pdf/valid.pdf, posted December 1998, accessed March 2012

(2) *Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis* (2012) *Official Methods of Analysis, Appendix D*, AOAC INTERNATIONAL, Gaithersburg, MD

(3) *AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Biological Threat Agent Methods and/or Procedures* (2012) *Official Methods of Analysis,* 19th Ed., *Appendix I, Calculation of CPOD and dCPOD Values from Qualitative Method Collaborative Study Data*, AOAC INTERNATIONAL, Gaithersburg, MD

(4) *AOAC Guidelines for Single-Laboratory Validation of Chemical Methods for Dietary Supplements and Botanicals* (2012) *Official Methods of Analysis*, 19th Ed., *Appendix K*, AOAC INTERNATIONAL, Gaithersburg, MD

(5) Codex Alimentarius Codex Procedure Manual

(6) International Organization for Standardization, Geneva, Switzlerland

ANNEX A
Format of a
Standard Method Performance Requirement

AOAC SMPR YYYY.XXX
(YYYY = Year; XXX = sequential identification number)

Method Name: Must include the analyte(s), matrix(es), and analytical technique [unless the standard method performance requirement (SMPR) is truly intended to be independent of the analytical technology]. The method name may refer to a "common" name (e.g., "Kjeldahl" method).

Approved By: Name of stakeholder panel or expert review panel

Final Version Date: Date

Effective Date: Date

1. Intended Use: Additional information about the method and conditions for use.

2. Applicability: List matrixes if more than one. Provide details on matrix such as specific species for biological analytes, or International Union of Pure and Applied Chemistry (IUPAC) nomenclature and Chemical Abstracts Service (CAS) registry number for chemical analytes. Specify the form of the matrix such as raw, cooked, tablets, powders, etc.

3. Analytical Technique: Provide a detailed description of the analytical technique if the SMPR is to apply to a specific analytical technique; or state that the SMPR applies to any method that meets the method performance requirements.

4. Definitions: List and define terms used in the performance parameter table (*see* Table A2 for list of standard terms).

5. Method Performance Requirements: List the performance parameters and acceptance criteria appropriate for each method/analyte/matrix. *See* Table A1 for appropriate performance requirements.

If more than one analyte/matrix, and if acceptance criteria differ for analyte/matrix combinations then organize a table listing each analyte/matrix combination and its minimum acceptance criteria for each performance criteria.

6. System Suitability Tests and/or Analytical Quality Control: Describe minimum system controls and QC procedures.

7. Reference Material(s): Identify the appropriate reference materials if they exist, or state that reference materials are not available. Refer to *Annex E* (*AOAC Method Accuracy Review*) for instructions on the use of reference materials in evaluations.

8. Validation Guidance: Recommendations for type of evaluation or validation program such as single-laboratory validation (SLV), *Official Methods of Analysis*℠ (OMA), or *Performance Tested Methods*℠ (PTM).

9. Maximum Time-to-Determination: Maximum allowable time to complete an analysis starting from the test portion preparation to final determination or measurement.

Annex I: Inclusivity/Selectivity Panel. Recommended for qualitative and identification method SMPRs.

Annex II: Exclusivity/Cross-Reactivity Panel. Recommended for qualitative and identification method SMPRs.

Annex III: Environmental Materials Panel. Recommended for qualitative and identification method SMPRs.

Table A1. Performance requirements

Classifications of methods[a]				
Quantitative method		Qualitative method		
Main component[b]	Trace or contaminant[c]	Main component[b]	Trace or contaminant[c]	Identification method
Parameter				
Single-laboratory validation				
Applicable range	Applicable range	Inclusivity/selectivity	Inclusivity/selectivity	Inclusivity/selectivity
Bias[d]	Bias[d]	Exclusivity/cross-reactivity	Exclusivity/cross-reactivity	Exclusivity/cross-reactivity
Precision	Precision	Environmental interference	Environmental interference	Environmental interference
Recovery	Recovery	Laboratory variance	Laboratory variance	
Limit of quantitation (LOQ)	LOQ			
		Probability of detection (POD)[e]	POD at AMDL[f]	Probability of identification (POI)
Reproducibility				
RSD_R or target measurement uncertainty	RSD_R or target measurement uncertainty	POD (0)	POD (0)	POI (c)
		POD (c)	POD (c)	
		Laboratory POD[g]	Laboratory POD[g]	Laboratory POI

[a] *See Annex B* for additional information on classification of methods.

[b] ≥100 g/kg.

[c] <100 g/kg.

[d] If a reference material is available.

[e] At a critical level.

[f] AMDL = Acceptable minimum detection level.

[g] LPOD = CPOD.

Table A2. Recommended definitions

Bias	Difference between the expectation of the test results and an accepted reference value. Bias is the total systematic error as contrasted to random error. There may be one or more systematic error components contributing to the bias.
Environmental interference	Ability of the assay to detect target organism in the presence of environmental substances and to be free of cross reaction from environmental substances.
Exclusivity	Strains or isolates or variants of the target agent(s) that the method must not detect.
Inclusivity	Strains or isolates or variants of the target agent(s) that the method can detect.
Laboratory probability of detection (POD)	Overall fractional response (mean POD = CPOD) for the method calculated from the pooled POD_j responses of the individual laboratories (j = 1, 2, ..., L).[a] *See Annex C*.
Limit of quantitation (LOQ)	Minimum concentration or mass of analyte in a given matrix that can be reported as a quantitative result.
POD (0)	Probability of the method giving a (+) response when the sample is truly without analyte.
POD (c)	Probability of the method giving a (–) response when the sample is truly without analyte.
POD	Proportion of positive analytical outcomes for a qualitative method for a given matrix at a given analyte level or concentration. Consult *Annex C* for a full explanation.
Probability of identification (POI)	Expected or observed fraction of test portions at a given concentration that gives positive result when tested at a given concentration. Consult *Probability of Identification (POI): A Statistical Model for the Validation of Qualitative Botanical Identification Methods*.[c]
Precision (repeatability)	Closeness of agreement between independent test results obtained under stipulated conditions. The measure of precision is usually expressed in terms of imprecision and computed as a standard deviation of the test results.[d]
Recovery	Fraction or percentage of the analyte that is recovered when the test sample is analyzed using the entire method. There are two types of recovery: (*1*) Total recovery based on recovery of the native plus added analyte, and (*2*) marginal recovery based only on the added analyte (the native analyte is subtracted from both the numerator and denominator).[e]
Repeatability	Precision under repeatability conditions.
Repeatability conditions	Conditions where independent test results are obtained with the same method on identical test items in the same laboratory by the same operator using the same equipment within short intervals of time.
Reproducibility	Precision under reproducibility conditions.
Reproducibility conditions	Conditions where independent test results are obtained with the same method on identical test items in different laboratories with different operators using different equipment.
Relative standard deviation (RSD)	$RSD = s_i \times 100/\bar{x}$
Standard deviation (s_i)	$s_i = [\Sigma(x_i - \bar{x})^2/n]^{0.5}$

[a] *AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Biological Threat Agent Methods and/or Procedures* (*Calculation of CPOD and dCPOD Values from Qualitative Method Collaborative Study Data*), *J. AOAC Int*. **94**, 1359(2011) and *Official Methods of Analysis of AOAC INTERNATIONAL* (2012) 19th Ed., *Appendix I*.

[b] *International Vocabulary of Metrology (VIM)—Basic and General Concepts and Associated Terms* (2008) JCGM 200:2008, Joint Committee for Guides in Metrology (JCGM), www.bipm.org

[c] LaBudde, R.A., & Harnly, J.M. (2012) *J. AOAC Int*. **95**, 273–285.

[d] ISO 5725-1-1994.

[e] *Official Methods of Analysis* (2012) *Appendix D* (*Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis*), AOAC INTERNATIONAL, Gaithersburg, MD.

Table A3. Recommendations for evaluation

Bias (if a reference material is available)	A minimum of five replicate analyses of a Certified Reference Material.[a]
Environmental interference	Analyze test portions containing a specified concentration of one environmental materials panel member. Materials may be pooled. Consult with AOAC statistician.
Exclusivity/cross-reactivity	Analyze one test portion containing a specified concentration of one exclusivity panel member. More replicates can be used. Consult with AOAC statistician.
Inclusivity/selectivity	Analyze one test portion containing a specified concentration of one inclusivity panel member. More replicates can be used. Consult with AOAC statistician.
Limit of quantitation (LOQ)	Estimate the LOQ = average (blank) + 10 × s_0 (blank). Measure blank samples with analyte at the estimated LOQ. Calculate the mean average and standard deviation of the results. Guidance[b]: For ML ≥ 100 ppm (0.1 mg/kg): LOD = ML × 1/5. For ML < 100 ppm (0.1 mg/kg): LOD = ML × 2/5.
Measurement uncertainty	Use ISO 21748: *Guidance for the use of repeatability, reproducibility, and trueness estimates in measurement uncertainty estimation to analyze data collected for bias, repeatability, and intermediate precision to estimate measurement uncertainty*.
POD(0)	Use data from collaborative study.
POD (c)	
Repeatability	Prepare and homogenize three unknown samples at different concentrations to represent the full, claimed range of the method. Analyze each unknown sample by the candidate method seven times, beginning each analysis from weighing out the test portion through to final result with no additional replication (unless stated to do so in the method). All of the analyses for one unknown sample should be performed within as short a period of time as is allowed by the method. The second and third unknowns may be analyzed in another short time period. Repeat for each claimed matrix.
Probability of detection (POD)	Determine the desired POD at a critical concentration. Consult with Table A7 to determine the number of test portions required to demonstrate the desired POD.
Probability of identification (POI)	Consult *Probability of Identification (POI): A Statistical Model for the Validation of Qualitative Botanical Identification Methods*[c].
Recovery	Determined from spiked blanks or samples with at least seven independent analyses per concentration level at a minimum of three concentration levels covering the analytical range. Independent means at least at different times. If no confirmed (natural) blank is available, the average inherent (naturally containing) level of the analyte should be determined on at least seven independent replicates. Marginal % recovery = $(C_f - C_u) \times 100/C_A$ Total % recovery = $100(C_f)/(C_u + C_A)$ where C_f = concentration of fortified samples, C_u = concentration of unfortified samples, and C_A = concentration of analyte added to the test sample.[d] Usually total recovery is used unless the native analyte is present in amounts greater than about 10% of the amount added, in which case use the method of addition.[e]
Reproducibility (collaborative or interlaboratory study)	Quantitative methods: Recruit 10–12 collaborators; must have eight valid data sets; two blind duplicate replicates at five concentrations for each analyte/matrix combination to each collaborator.
	Qualitative methods: Recruit 12–15 collaborators; must have 10 valid data sets; six replicates at five concentrations for each analyte/matrix combination to each collaborator.

[a] *Guidance for Industry for Bioanalytical Method Validation* (May 2001) U.S. Department of Health and Human Services, U.S. Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM).

[b] Codex Alimentarius Codex Procedure Manual.

[c] LaBudde, R.A., & Harnly, J.M. (2012) *J. AOAC Int.* **95**, 273–285.

[d] *Guidelines for Collaborative Study Procedures to Validate Characteristics of a Method of Analysis* (2012) *Official Methods of Analysis*, 19th Ed., *Appendix D,* AOAC INTERNATIONAL, Gaithersburg, MD.

[e] *AOAC Guidelines for Single-Laboratory Validation of Chemical Methods for Dietary Supplements and Botanicals* (2012) *Official Methods of Analysis*, 19th Ed., *Appendix K*, AOAC INTERNATIONAL, Gaithersburg, MD.

Table A4. Expected precision (repeatability) as a function of analyte concentration[a]

Analyte, %	Analyte ratio	Unit	RSD, %
100	1	100%	1.3
10	10^{-1}	10%	1.9
1	10^{-2}	1%	2.7
0.01	10^{-3}	0.1%	3.7
0.001	10^{-4}	100 ppm (mg/kg)	5.3
0.0001	10^{-5}	10 ppm (mg/kg)	7.3
0.00001	10^{-6}	1 ppm (mg/kg)	11
0.000001	10^{-7}	100 ppb (µg/kg)	15
0.0000001	10^{-8}	10 ppb (µg/kg)	21
0.00000001	10^{-9}	1 ppb (µg/kg)	30

[a] Table excerpted from *AOAC Peer-Verified Methods Program, Manual on Policies and Procedures* (1998) AOAC INTERNATIONAL, Gaithersburg, MD.

The precision of a method is the closeness of agreement between independent test results obtained under stipulated conditions. Precision is usually expressed in terms of imprecision and computed as a relative standard deviation of the test results. The imprecision of a method increases as the concentration of the analyte decreases. This table provides targets RSDs for a range of analyte concentrations.

Table A5. Expected recovery as a function of analyte concentration[a]

Analyte, %	Analyte ratio	Unit	Mean recovery, %
100	1	100%	98–102
10	10^{-1}	10%	98–102
1	10^{-2}	1%	97–103
0.01	10^{-3}	0.1%	95–105
0.001	10^{-4}	100 ppm	90–107
0.0001	10^{-5}	10 ppm	80–110
0.00001	10^{-6}	1 ppm	80–110
0.000001	10^{-7}	100 ppb	80–110
0.0000001	10^{-8}	10 ppb	60–115
0.00000001	10^{-9}	1 ppb	40–120

[a] Table excerpted from *AOAC Peer-Verified Methods Program, Manual on Policies and Procedures* (1998) AOAC INTERNATIONAL, Gaithersburg, MD.

Recovery is defined as the ratio of the observed mean test result to the true value. The range of the acceptable mean recovery expands as the concentration of the analyte decreases. This table provides target mean recovery ranges for analyte concentrations from 100% to 1 ppb.

Table A6. Predicted relative standard deviation of reproducibility ($PRSD_R$)[a]

Concentration (C)	Mass fraction (C)	$PRSD_R$, %
100%	1.0	2
1%	0.01	4
0.01%	0.0001	8
1 ppm	0.000001	16
10 ppb	0.00000001	32
1 ppb	0.000000001	45

[a] Table excerpted from *Definitions and Calculations of HorRat Values from Intralaboratory Data*, HorRat for SLV.doc, 2004-01-18, AOAC INTERNATIONAL, Gaithersburg, MD.

Predicted relative standard deviation = $PRSD_R$. Reproducibility relative standard deviation calculated from the Horwitz formula:

$$PRSD_R = 2C^{-0.15}, \text{ where C is expressed as a mass fraction}$$

This table provides the calculated $PRSD_R$ for a range of concentrations. *See Annex D* for additional information.

Table A7. POD and number of test portions[a,b]

	Sample size required for proportion						
Assume	1. Binary outcome (occur/not occur). 2. Constant probability rho of event occurring. 3. Independent trials (e.g., simple random sample). 4. Fixed number of trials (*N*)						
Inference	95% Confidence interval lies entirely at or above specified minimum rho						
Desired	Sample size *N* needed						
Minimum probability rho, %	Sample size (*N*)	Minimum No. events (*x*)	Maximum No. nonevents (*y*)	1-Sided lower confidence limit on rho[c], %	Expected lower confidence limit on rho, %	Expected upper confidence limit on rho, %	Effective AOQL[d] rho, %
50	3	3	0	52.6	43.8	100.0	71.9
50	10	8	2	54.1	49.0	94.3	71.7
50	20	14	6	51.6	48.1	85.5	66.8
50	40	26	14	52.0	49.5	77.9	63.7
50	80	48	32	50.8	49.0	70.0	59.5
55	4	4	0	59.7	51.0	100.0	75.5
55	10	9	1	65.2	59.6	100.0	79.8
55	20	15	5	56.8	53.1	88.8	71.0
55	40	28	12	57.1	54.6	81.9	68.2
55	80	52	28	55.9	54.1	74.5	64.3
60	5	5	0	64.9	56.5	100.0	78.3
60	10	9	1	65.2	59.6	100.0	79.8
60	20	16	4	62.2	58.4	91.9	75.2
60	40	30	10	62.4	59.8	85.8	72.8
60	80	56	24	61.0	59.2	78.9	69.1
65	6	6	0	68.9	61.0	100.0	80.5
65	10	9	1	65.2	59.6	100.0	79.8
65	20	17	3	67.8	64.0	94.8	79.4
65	40	31	9	65.1	62.5	87.7	75.1
65	80	59	21	65.0	63.2	82.1	72.7
70	7	7	0	72.1	64.6	100.0	82.3
70	10	10	0	78.7	72.2	100.0	86.1
70	20	18	2	73.8	69.9	97.2	83.6
70	40	33	7	70.7	68.0	91.3	79.7
70	80	63	17	70.4	68.6	86.3	77.4
75	9	9	0	76.9	70.1	100.0	85.0
75	10	10	0	78.7	72.2	100.0	86.1
75	20	19	1	80.4	76.4	100.0	88.2
75	40	35	5	76.5	73.9	94.5	84.2
75	80	67	13	75.9	74.2	90.3	82.2
80	11	11	0	80.3	74.1	100.0	87.1
80	20	19	1	80.4	76.4	100.0	88.2
80	40	37	3	82.7	80.1	97.4	88.8
80	80	70	10	80.2	78.5	93.1	85.8
85	20	20	0	88.1	83.9	100.0	91.9
85	40	38	2	86.0	83.5	98.6	91.1
85	80	74	6	86.1	84.6	96.5	90.6
90	40	40	0	93.7	91.2	100.0	95.6
90	60	58	2	90.4	88.6	99.1	93.9
90	80	77	3	91.0	89.5	98.7	94.1
95	60	60	0	95.7	94.0	100.0	97.0
95	80	80	0	96.7	95.4	100.0	97.7
95	90	89	1	95.2	94.0	100.0	97.0
95	96	95	1	95.5	94.3	100.0	97.2
98	130	130	0	98.0	97.1	100.0	98.6
98	240	239	1	98.2	97.7	100.0	98.8
99	280	280	0	99.0	98.6	100.0	99.3
99	480	479	1	99.1	98.8	100.0	99.4

[a] Table excerpted from Technical Report TR308, *Sampling plans to verify the proportion of an event exceeds or falls below a specified value*, LaBudde, R. (June 4, 2010) (not published). The table was produced as part of an informative report for the Working Group for Validation of Identity Methods for Botanical Raw Materials commissioned by the AOAC INTERNATIONAL Presidential Task Force on Dietary Supplements. The project was funded by the Office of Dietary Supplements, National Institutes of Health.

[b]

[c] Based on modified Wilson score 1-sided confidence interval.

[d] AOQL = Average outgoing quality level.

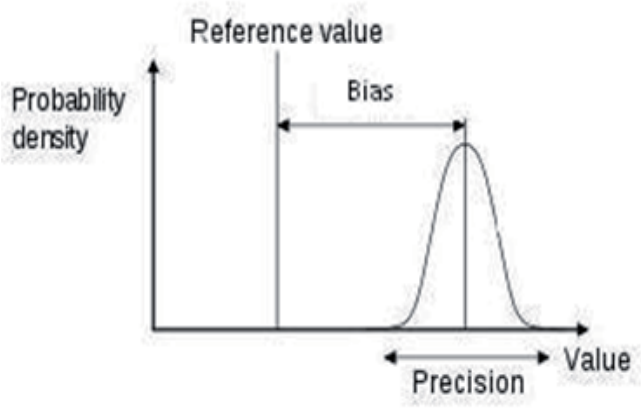


Figure A1. Relationship between precision versus bias (trueness). Trueness is reported as bias. Bias is defined as the difference between the test results and an accepted reference value.

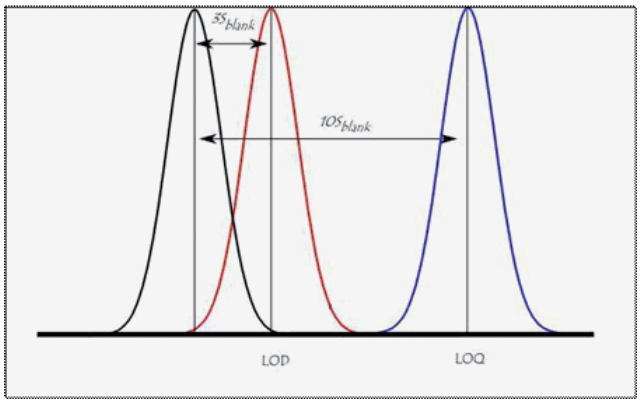


Figure A2. Relationship between LOD and LOQ. LOD is defined as the lowest quantity of a substance that can be distinguished from the absence of that substance (a blank value) within a stated confidence limit. LOQ is the level above which quantitative results may be obtained with a stated degree of confidence.

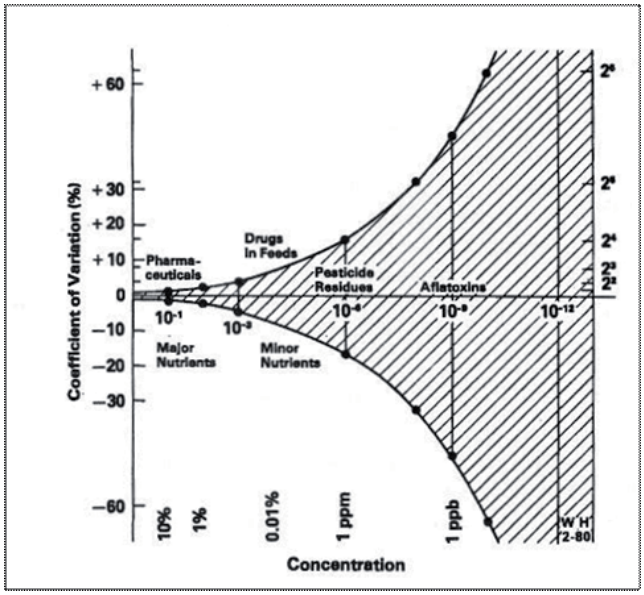


Figure A3. Horwitz Curve, illustrating the exponential increase in the coefficient of variation as the concentration of the analyte decreases [*J. AOAC Int*. 89, 1095(2006)].

ANNEX B
Classification of Methods

The following guidance may be used to determine which performance parameters in Table A1 apply to different classifications of methods. AOAC INTERNATIONAL does not recognize the term "semiquantitative" as a method classification. Methods that have been self-identified as semiquantitative will be classified into one of the following five types:

Type I: Quantitative Methods

Characteristics: Generates a continuous number as a result.

Recommendation: Use performance requirements specified for quantitative method (main or trace component). Use recovery range and maximum precision variation in Tables A4 and A5.

In some cases and for some purposes, methods with less accuracy and precision than recommended in Tables A4 and A5 may be acceptable. Method developers should consult with the appropriate method committee to determine if the recommendations in Tables A4 and A5 do or do not apply to their method.

Type II: Methods that Report Ranges

Characteristics: Generates a "range" indicator such as 0, low, moderate, and high.

Recommendation: Use performance requirements specified for qualitative methods (main component). Specify a range of POD for each range "range" indicator.

Type III: Methods with Cutoff Values

Characteristics: Method may generate a continuous number as an interim result (such as a CT value for a PCR method), which is not reported but converted to a qualitative result (presence/ absence) with the use of a cutoff value.

Recommendation: Use performance requirements specified for qualitative methods.

Type IV: Qualitative Methods

Characteristics: Method of analysis whose response is either the presence or absence of the analyte detected either directly or indirectly in a specified test portion.

Recommendation: Use performance requirements specified for qualitative methods.

Type V: Identification Methods

Characteristics: Method of analysis whose purpose is to determine the identity of an analyte.

Recommendation: Use performance requirements specified for identification methods.

ANNEX C
Understanding the POD Model

Excerpted from AOAC INTERNATIONAL Methods Committee Guidelines for Validation of Biological Threat Agent Methods and/or Procedures, J. AOAC Int. ***94****, 1359(2011) and Official Methods of Analysis of AOAC INTERNATIONAL (2012) 19th Ed., Appendix I.*

The Probability of Detection (POD) model is a way of characterizing the performance of a qualitative (binary) method. A binary qualitative method is one that gives a result as one of two possible outcomes, either positive or negative, presence/absence, or +/–.

The single parameter of interest is the POD, which is defined as the probability at a given concentration of obtaining a positive response by the detection method. POD is assumed to be dependent on concentration, and generally, the probability of a positive response will increase as concentration increases.

For example, at very low concentration, the expectation is that the method will not be sensitive to the analyte, and at very high concentration, a high probability of obtaining a positive response is desired. The goal of method validation is to characterize how method response transitions from low concentration/low response to high concentration/high response.

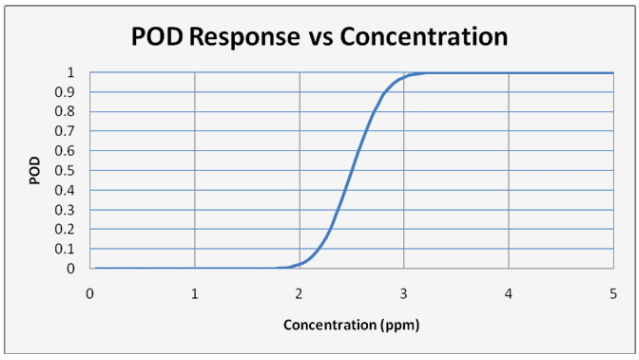


Figure C1. Theoretical POD curve for a qualitative detection method.

POD is always considered to be dependent upon analyte concentration. The POD curve is a graphical representation of method performance, where the probability is plotted as a function of concentration (*see*, for example, Figure C1).

The POD model is designed to allow an objective description of method response without consideration to an a priori expectation of the probabilities at given concentrations. The model is general enough to allow comparisons to any theoretical probability function.

The POD model is also designed to allow for an independent description of method response without consideration to the response of a reference method. The model is general enough to allow for comparisons between reference and candidate method responses, if desired.

Older validation models have used the terms "sensitivity," "specificity," "false positive," and "false negative" to describe method performance. The POD model incorporates all of the performance concepts of these systems into a single parameter, POD.

For example, false positive has been defined by some models as the probability of a positive response, given the sample is truly negative (concentration = 0). The equivalent point on the POD curve for this performance characteristic is the value of the curve at Conc = 0.

Similarly, false negative has sometimes been defined as the probability of a negative response when the sample is truly positive (concentration >0). In the POD curve, this would always be specific to a given sample concentration, but would be represented as the distance from the POD curve to the POD = 1 horizontal top axis at all concentrations except C = 0.

The POD model incorporates all these method characteristics into a single parameter, which is always assumed to vary by concentration. In other models, the terms "false positive," "false negative," "sensitivity," and "specificity" have been defined in a variety of ways, usually not conditional on concentration. For these reasons, these terms are obsolete under this model (*see* Table C1).

The terms "sensitivity," "specificity," "false positive," and "false negative" are obsolete under the POD model (*see* Figure C2).

Table C1. Terminology

Traditional terminology	Concept	POD equivalent	Comment
False positive	Probability of the method giving a (+) response when the sample is truly without analyte	POD(0) POD at conc = 0	POD curve value at conc = 0; "*Y*-intercept" of the POD curve
Specificity	Probability of the method giving a (-) response when the sample is truly without analyte	1-POD(0)	Distance along the POD axis from POD = 1 to the POD curve value
False negative (at a given concentration)	Probability of a (–) response at a given concentration	1-POD(c)	Distance from the POD curve to the POD = 1 "top axis" in the vertical direction
Sensitivity (at a given concentration)	Probability of a (+) response at a given concentration	POD(c)	Value of the POD curve at any given concentration
True negative	A sample that contains no analyte	C = 0	Point on concentration axis where c = 0
True positive	A sample that contains analyte at some positive concentration	C > 0	Range of concentration where c > 0

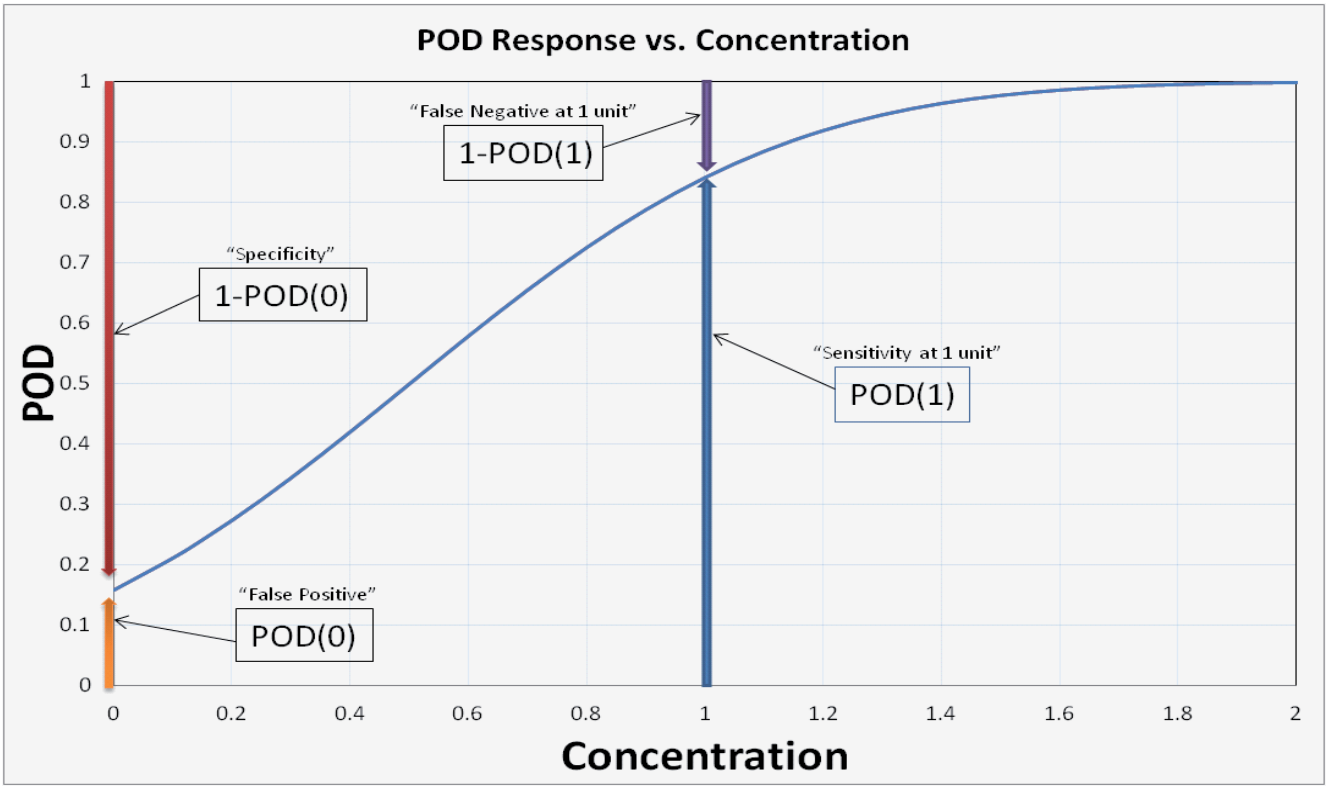


Figure C2. Comparison of POD model terminology to other obsolete terms.

ANNEX D
Definitions and Calculations of HorRat Values from Intralaboratory Data

Excerpted from Definitions and Calculations of HorRat Values from Intralaboratory Data, AOAC INTERNATIONAL, HorRat for SLV.doc, 2004-01-18.

1. Definitions

1.1 Replicate Data

Data developed under common conditions in the same laboratory: simultaneous performance, or, if necessary to obtain sufficient values, same series, same analyst, same day. Such data provides "repeatability statistical parameters."

1.2 Pooled Data

Replicate data developed in the same laboratory under different conditions but considered sufficiently similar that, for the purpose of statistical analysis, they may be considered together. These may include different runs, different instruments, different analysts, and different days.

1.3 Average

0 = Sum of the individual values, x_i, divided by the number of individual values, *n*.

$$0 = (\Sigma\, x_i)/n$$

1.4 Standard Deviation

$$s_i = [\Sigma(x_i - (\bar{x})^2/n]^{0.5}$$

1.5 Relative Standard Deviation

$$RSD = s_i \times 100/\bar{x}$$

1.5.1 Repeatability Relative Standard Deviation [RSD(r) or RSD_r]

The relative standard deviation calculated from within-laboratory data.

1.5.2 Reproducibility Relative Standard Deviation [RSD(R) or RSD_R]

The relative standard deviation calculated from among-laboratory data.

Table D1. Predicted relative standard deviations

Concentration (C)	Mass fraction (C)	$PRSD_R$, %
100%	1.0	2
1%	0.01	4
0.01%	0.0001	8
1 ppm	0.000001	16
10 ppb	0.00000001	32
1 ppb	0.000000001	45

1.6 Mass Fraction

Concentration, C, expressed as a decimal fraction. For calculating and reporting statistical parameters, data may be expressed in any convenient units (e.g., %, ppm, ppb, mg/g, µg/g; µg/kg; µg/L, µg/µL, etc.). For reporting HorRat values, data must be reported as a mass fraction where the units of the numerator and denominator are the same: e.g., for 100% (pure materials), the mass fraction C = 1.00; for 1 µg/g (ppm), C = 0.000001 = (E-6). *See* Table D1 for other examples.

1.7 Predicted Relative Standard Deviation [PRSD(R) or $PRSD_R$]

The reproducibility relative standard deviation calculated from the Horwitz formula:

$$PRSD(R) = 2C^{-0.15}$$

where C is expressed as a mass fraction. *See* Table D1.

In spreadsheet notation: PRSD(R) = 2 * C ^(–0.15).

1.8 HorRat Value

The ratio of the reproducibility relative standard deviation calculated from the data to the PRSD(R) calculated from the Horwitz formula:

$$HorRat = RSD(R)/PRSD(R)$$

To differentiate the usual HorRat value calculated from reproducibility data from the HorRat value calculated from repeatability data, attach an R for the former and an r for the latter. But note that the denominator always uses the PRSD(R) calculated from reproducibility data because this parameter is more predictable than the parameter calculated from repeatability data:

$$HorRat(R) = RSD_R/PRSD(R)$$

$$HorRat(r) = RSD_r/PRSD(R)$$

Some expected, predicted relative standard deviations are given in Table D1.

2 *Acceptable HorRat Values*

2.1 For Interlaboratory Studies

HorRat(R): The original data developed from interlaboratory (among-laboratory) studies assigned a HorRat value of 1.0 with limits of acceptability of 0.5 to 2.0. The corresponding within-laboratory relative standard deviations were found to be typically 1/2 to 2/3 the among-laboratory relative standard deviations.

Table D2. Predicted relative standard deviations

Concentration (C)	$PRSD_R$, %	$PRSD_r$, %
100%	2	1
1%	4	2
0.01%	8	4
1 ppm	16	8
10 ppb	32	16
1 ppb	45	22

2.1.1 Limitations

HorRat values do not apply to method-defined (empirical) analytes (moisture, ash, fiber, carbohydrates by difference, etc.), physical properties or physical methods (pH, viscosity, drained weight, etc.), and ill-defined analytes (polymers, products of enzyme reactions).

2.2 For Intralaboratory Studies

2.2.1 Repeatability

Within-laboratory acceptable predicted target values for repeatability are given in Table D2 at 1/2 of PRSD(R), which represents the best case.

2.2.2 HorRat(r)

Based on experience and for the purpose of exploring the extrapolation of HorRat values to SLV studies, take as the minimum acceptability 1/2 of the lower limit ($0.5 \times 0.5 \approx 0.3$) and as the maximum acceptability 2/3 of the upper limit ($0.67 \times 2.0 \approx 1.3$).

Calculate HorRat(r) from the SLV data:

$$HorRat(r) = RSD(r)/PRSD(R)$$

Acceptable HorRat(r) values are 0.3–1.3. Values at the extremes must be interpreted with caution. With a series of low values, check for unreported averaging or prior knowledge of the analyte content; with a series of high values, check for method deficiencies such as unrestricted times, temperatures, masses, volumes, and concentrations; unrecognized impurities (detergent residues on glassware, peroxides in ether); incomplete extractions and transfers and uncontrolled parameters in specific instrumental techniques.

2.3 Other Limitations and Extrapolations

The HorRat value is a very rough but useful summary of the precision in analytical chemistry. It overestimates the precision at the extremes, predicting more variability than observed at the high end of the scale (C > ca 0.1; i.e., >10%) and at the low end of the scale (C < E-8; i.e., 10 ng/g; 10 ppb).

ANNEX E
AOAC Method Accuracy Review

Accuracy of Method Based on Reference Material

Reference material (RM) used.—The use of RMs should be seen as integral to the process of method development, validation, and performance evaluation. RMs are not the only component of a quality system, but correct use of RMs is essential to appropriate quality management. RMs with or without assigned quantity values can be used for measurement precision control, whereas only RMs with assigned quantity values can be used for calibration or measurement trueness control. Method development and validation for matrices within the scope of the method is done to characterize attributes such as recovery, selectivity, "trueness" (accuracy, bias), precision (repeatability and reproducibility), uncertainty estimation, ruggedness, LOQ or LOD, and dynamic range. RMs should be chosen that are fit-for-purpose. When certified reference materials (CRMs) are available with matrices that match the method scope, much of the work involved in method development has already been completed, and that work is documented through the certificate. RMs with analyte values in the range of test samples, as well as "blank" matrix RMs, with values below or near detection limits, are needed.

Availability of RM.—Consideration needs to be given to the future availability of the chosen RM. Well-documented methods that cannot be verified in the future due to lack of material may lose credibility or be seen as inferior.

Fit to method scope.—Natural matrix CRMs provide the greatest assurance that the method is capable of producing accurate results for that matrix. When selecting an RM to perform a method validation, analysts should consider the method to material fit. An example of a good fit would be a method for specified organic molecules in infant formula and using an infant formula or powder milk RM. A poor fit would be a method for specified organic molecules in infant formula and using a sediment material.

Stability.—Providing a stable RM can be challenging where analytes are biologically active, easily oxidized, or interactive with other components of the matrix. CRM producers provide assurance of material stability, as well as homogeneity.CRMs are accompanied by a certificate that includes the following key criteria:

(*1*) Assigned values with measurement uncertainty and metrological traceability
(*2*) Homogeneity
(*3*) Stability, with the expiration date for the certificate
(*4*) Storage requirements
(*5*) Information on intended use
(*6*) Identity of matrix

For some RMs, such as botanical RMs, the source and/or authenticity can be a very important piece of information that should be included with the certificate. Even under ideal storage conditions, many analytes have some rate of change. Recertification may be done by the supplier, and a certificate reissued with a different expiration date and with certain analyte data updated or removed.

Definition of CRM.—Refer to the AOAC TDRM document for definitions from ISO Guide 30, Amd. 1 (2008), http://www.aoac.org/divisions/References.pdf.

Information on source of RM is available.—It is the responsibility of the material producer to provide reliable authentication of the RM and make a clear statement in the accompanying documentation. This should be an as detailed listing as possible, including handling of ingredients, identification of plant materials as completely as feasible (species, type, subtype, growing region), etc. This is comparable to other required information on an RM for judging its suitability for a specific application purpose (e.g., containing how much of the targeted analyte, stabilized by adding acid—therefore not suited for certain parameters/procedures, etc.).

Separate RM used for calibration and validation.—A single RM cannot be used for both calibration and validation of results in the same measurement procedure.

Blank RM used where appropriate.—Blank matrix RMs are useful for ensuring performance at or near the detection limits. These are particularly useful for routine quality control in methods measuring, for instance, trace levels of allergens, mycotoxins, or drug residues.

Storage requirements were maintained.—Method developers should maintain good documentation showing that the RM producer's recommended storage conditions were followed.

Cost.—The cost of ongoing method checks should be considered. Daily use of CRMs can be cost prohibitive. Monthly or quarterly analysis of these materials may be an option.

Concentration of analyte fits intended method.—Concentration of the analyte of interest is appropriate for standard method performance requirements (SMPRs).

Uncertainty available.—Every measurement result has an uncertainty associated with it, and the individual contributions toward the combined uncertainty arise from multiple sources. Achieving the target measurement uncertainty set by the customer for his/her problem of interest is often one of the criteria used in selecting a method for a given application. Estimation of measurement uncertainty can be accomplished by different approaches, but the use of RMs greatly facilitates this part of a method validation.

Demonstration of Method Accuracy when No Reference Material Is Available

If an RM is not available, how is accuracy demonstrated?

There are many analytes for which a CRM with a suitable matrix is not available. This leaves the analyst with few options. For some methods, there may be proficiency testing programs that include a matrix of interest for the analyte. Proficiency testing allows an analyst to compare results with results from other laboratories, which may or may not be using similar methods. Spiking is another technique that may be used. When alternative methods are available, results may be compared between the different methods. These alternatives do not provide the same level of assurance that is gained through the use of a CRM.

Spike recovery.—In the absence of an available CRM, one technique that is sometimes used for assessing performance is the spiking of a matrix RM with a known quantity of the analyte. When this method is used, it cannot be assumed that the analyte is bound in the same way as it would be in a natural matrix. Nevertheless, a certified blank RM would be the preferred choice for constructing a spiked material.

When preparing reference solutions, the pure standards must be completely soluble in the solvent. For insoluble materials in a liquid suspension or for powdered forms of dry materials, validation is required to demonstrate that the analyte is homogeneously distributed and that the response of the detection system to the analyte is not affected by the matrix or preparation technique. When a matrix material is selected for spiking, it should be reasonably

The document, *AOAC Method Accuracy Review*, was prepared by the AOAC Technical Division on Reference Materials (TDRM) and approved by the AOAC Official Methods Board in June 2012.

characterized to determine that it is sufficiently representative of the matrix of interest. Spiked samples must be carried through all steps of the method. Many analytes are bound in a natural matrix and whether the spiked analyte will behave the same as the analyte in a natural matrix is unknown.

Other.—Use of a substitute RM involves the replacement of the CRM with an alternative matrix RM matching the matrix of interest as close as possible based on technical knowledge.

ANNEX F
Development and Use of In-House Reference Materials

The use of reference materials is a vital part of any analytical quality assurance program. However, you may have questions about their creation and use. The purpose of this document is to help answer many of these questions.

- What is a reference material?
- Why use reference materials?
- What certified reference materials are currently available?
- Why use an in-house reference material?
- How do I create an in-house reference material?
- How do I use the data from an in-house reference material?

What Is a Reference Material?

The International Organization for Standardization (ISO) defines a reference material as a "material or substance one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials" (1). In plain English, natural-matrix reference materials, such as those you might prepare for use in-house, can be used to validate an analytical method or for quality assurance while you're using your method to analyze your samples. (Natural-matrix materials are not generally used as calibrants because of the increased uncertainty that this would add to an analysis.) The assigned values for the target analytes of an in-house reference material can be used to establish the precision of your analytical method and, if used in conjunction with a CRM, to establish the accuracy of your method.

ISO defines a certified reference material (CRM) as a "reference material, accompanied by a certificate, one or more of whose property values are certified by a procedure which establishes traceability to an accurate realization of the unit in which the property values are expressed, and for which each certified value is accompanied by an uncertainty at a stated level of confidence" (1).

Why Use Reference Materials?

Certified reference materials can be used across the entire scope of an analytical method and can provide traceability of results to the International System of Units (SI). During method development, CRMs can be used to optimize your method. During method validation, they can be used to ensure that your method is capable of producing the "right" answer, and to determine how close your result is to that answer. During routine use, they can be used to determine within-day and between-day repeatability, and so demonstrate that your method is in control and is producing accurate results every time it is used.

Natural-matrix reference materials should mimic the real samples that will be analyzed with a method. They should behave just as your samples would during a procedure, so if you obtain accurate and precise values for your reference material, you should obtain accurate and precise values for your samples as well.

What Certified Reference Materials Are Currently Available?

CRMs are available from a number of sources, including (but not limited to):

- American Association of Cereal Chemists (AACC)
- American Oil Chemists Society (AOCS)
- International Atomic Energy Agency (IAEA)
- Institute for Reference Materials and Measurements (IRMM)
- LGC Promochem
- National Institute of Standards and Technology (NIST)
- National Research Council Canada (NRC Canada)
- UK Food Analysis Proficiency Assessment Program (FAPAS)

A number of websites provide general overviews and catalogs of producers' and distributors' reference materials:

http://www.aocs.org/tech/crm/
http://www.comar.bam.de
http://www.erm-crm.org
http://www.iaea.org/oregrammeslaqcs
http://www.aaccnet.org/checksample
http://www.irmm·ire.be/mrm.html
http://www.lgcpromochem.com
http://www.naweb.iaea.org/nahu/nmrm/
http://www.nist.gov/srm
http://www.fapas.com/index. cfm
http://www.virm.net.

Because new reference materials are produced regularly, it is important to check these websites to determine what is currently available.

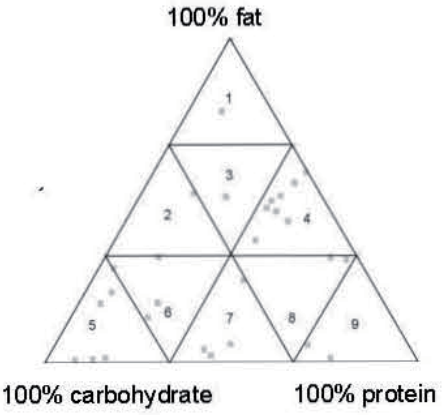
Why Use an In-House Reference Material?

There are many benefits to the use of a CRM. CRMs have been prepared to be homogeneous and, if stored under the proper conditions, stable. You are provided with a certified value as well as the statistical data for theconcentration of your analyte; this is about as close as you can come to knowing the true value of the concentration of the analyte. The material has been tested by experienced analysts in leading laboratories, so you have the security of knowing that your method is generating values similar to those generated in other competent laboratories. The CRMs from the sources mentioned above are nationally and/or internationally recognized, so when you obtain acceptable results for a CRM using your analytical method, you give credibility to your methodology and traceability to your results.

But there are some drawbacks associated with CRMs. Unfortunately, many analyte/matrix combinations are not currently available. When testing food products for nutrient content, for example, a laboratory can be asked to analyze anything that might be found in a kitchen or grocery store. Reference materials that represent all of the types of foods that need to be tested are not available, and most CRMs are certified for a limited number of analytes. It is important to match the reference material matrix to your sample matrix. (Food examples dominate the discussion below, but the same processes apply to the development of in-house RMs in other areas of analytical chemistry.)

To demonstrate the applicability of an analytical method to a wide variety of food matrices, AOAC INTERNATIONAL's Task

Excerpted from *Development and Use of In-House Reference Materials*, Rev. 2, 2009. Copyright 2005 by the AOAC Technical Division on Reference Materials (TDRM).



Force on Methods for Nutrition Labeling developed a triangle partitioned into sectors in which foods are placed based on their protein, fat, and carbohydrate content (2, 3). Since ash does not have a great impact on the performance of an analytical method for organic-material foods, and water can be added or removed, it can be assumed that the behavior of an analytical method is determined to large extent by the relative proportions of these proximates. AOAC INTERNATIONAL anticipated that one or two foods in a given sector would be representative of other foods in that sector and therefore would be useful for method assessment. Similarly, one or two reference materials in a given sector (or near each other in adjacent sectors) should be useful for quality assurance for analyses involving the other foods in the sector. The positions of many of the food-matrix CRMs from the sources listed above are shown in the triangle and are provided in the list.

These food-matrix reference materials are spread through all sectors of the triangle, thereby making it likely that you can find an appropriate CRM to match to your samples. Ultimately, however, the routine use of a CRM can be cost prohibitive, and is not really the purpose of CRMs. For example, in order to use NIST's Standard Reference Material (SRM) 2387 Peanut Butter for all mandatory nutrition labeling analyses, you could buy one sales unit (three jars, each containing 170 g material) for $649 (2009 price). If you charge your customer about $1000 for analysis of all mandatory nutrients in a test material, the control material would account for more than 60% of your fees. Therefore, many laboratories have found it more cost-effective to create in-house reference materials for routine quality control and characterize them in conjunction with the analysis of a CRM (4). You can prepare larger quantities of a reference material by preparing it in-house, and you have more flexibility in the types of matrices you can use. There are not many limitations on what can be purchased.

How Do I Create an In-House Reference Material?

There are basically three steps to preparing an in-house reference material: selection (including consideration of homogeneity and stability), preparation, and characterization. Additional guidance through these steps can be provided from TDRM as well as in ISO Guides 34 (5) and 35 (6).

References

(1) JCGM 200:2008, *International vocabulary of metrology—Basic and general concepts and associated terms (VIM)*, International Bureau of Weights and Measures (www.bipm.org)

Sector	RM No.	Matrix
	NIST 1563	Coconut oil
1	NIST 3274	Fatty acids in botanical oils
1	NIST 3276	Carrot extract in oil
1	LGC 7104	Sterilized cream
2	NIST 2384	Baking chocolate
3	NIST 2387	Peanut butter
4	NIST 1546	Meat homogenate
4	LGC 7106	Processed cheese
4	LGC 7000	Beef/pork meat
4	LGC 7150	Processed meat
4	LGC 7151	Processed meat
4	LGC 7152	Processed meat
4	SMRD 2000	Fresh meat
4	LGC 7101	Mackerel paste
4	LGC QC1001	Meat paste 1
4	LGC QC1004	Fish paste 1
5	BCR-382	Wleat flour
5	BCR-381	Rye flour
5	LGC 7103	Sweet digestive biscuit
5	LGC 7107	Madeira cake
5	LGC QC1002	Flour 1
6	NIST 1544	Fatty acids
6	NIST 1548a	Typical diet
6	NIST 1849	Infant/adult nutritional formula
6	LGC 7105	Rice pudding
7	LGC 7001	Pork meat
7	NIST 1566b	Oyster tissue
7	NIST 1570a	Spinach leaves
7	NIST 2385	Spinach
8	NIST 1946	Lake trout
8	LGC 7176	Canned pet food
9	NIST 1974a	Mussel tissue
9	NIST 3244	Protein powder

(2) Wolf, W.R., & Andrews, K.W. (1995) *Fresenius' J. Anal. Chem.* **352**, 73–76

(3) Wolf, W.R. (1993) *Methods of Analysis for Nutrition Labeling*, D.R. Sullivan & D.E. Carpenter (Eds), AOAC INTERNATIONAL, Gaithersburg, MD

(4) European Reference Materials (2005) *Comparison of a Measurement Result with the Certified Value*, Application Note 1

(5) *ISO Guide 34 General Requirements for the Competence of Reference Material Producers* (2009) 2nd, International Organization for Standardization, Geneva, Switzerland

(6) *Guide 35 Certification of Reference Materials—General and Statistical Principles* (2006) International Organization for Standardization, Geneva, Switzerland

For more information about the AOAC Technical Division on Reference Materials, visit http://aoac.org/divisions/tdrm.

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.

(*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.

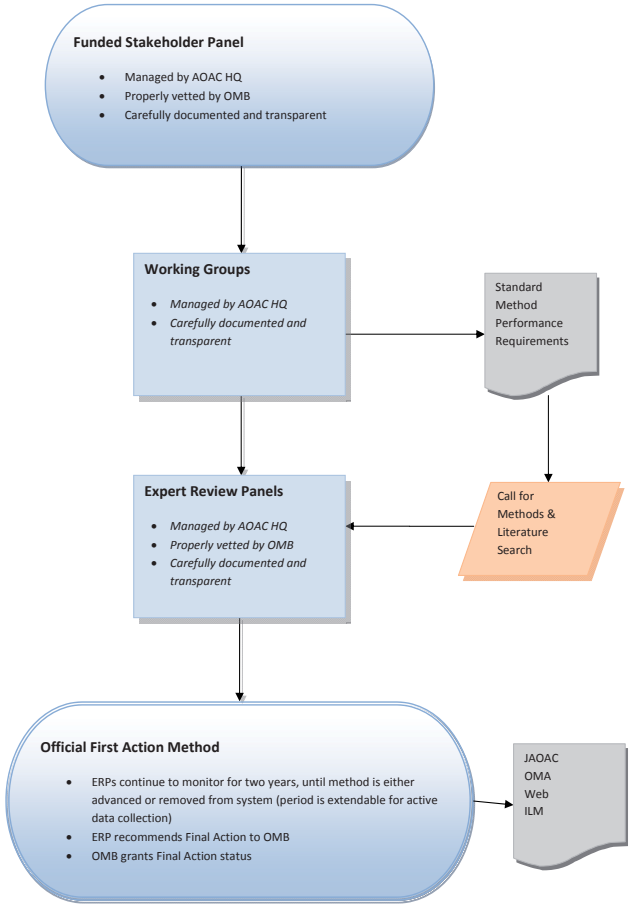


Figure 1. Summary of standards development through *Official Methods of Analysis*.

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.

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.

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.

* * * * * *

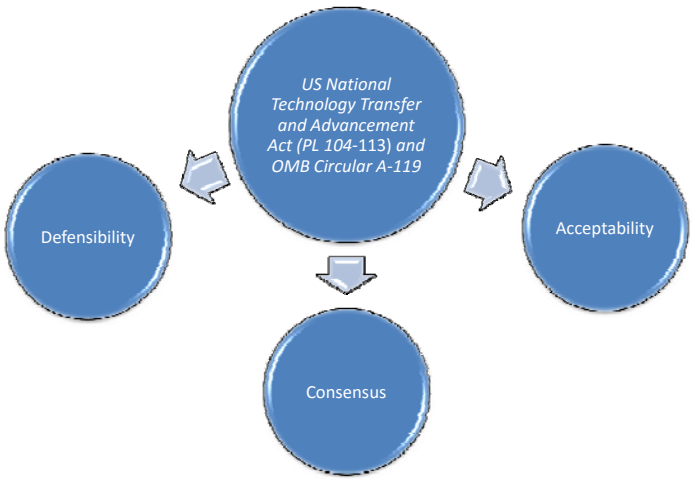
Adopted by the AOAC Board of Directors: September 24, 1989
Revised: June 13, 1991; February 26, 1992; March 21, 1995; October 1996

AOAC Stakeholder Panel on Strategic Food Analytical Methods

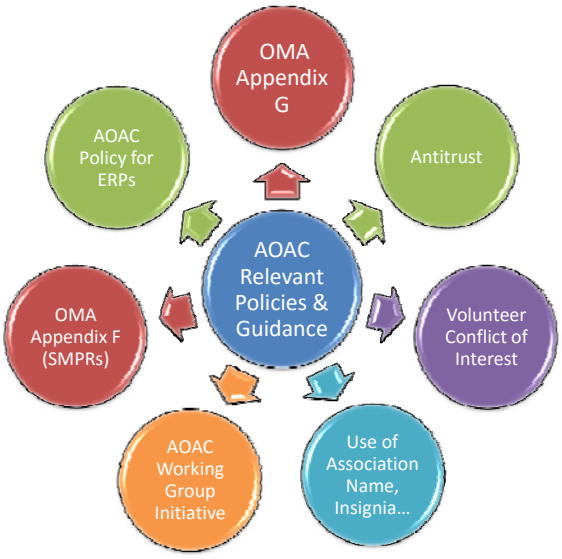
AOAC Standards Development Process

Launch of AOAC Stakeholder Panel Working Groups

AOAC Standard Development Process



AOAC Standards Development



SMPR® is a registered trademark of AOAC INTERNATIONAL

AOAC Standards Development

- AOAC develops voluntary consensus standards using the following principles:

Transparency
Openness
Balance
Due Process
Consensus
Appeals

Stakeholder Panel Activity

June 2016
- Define specific analytical issues
- Ocean Spray began WG Initiative for Proanthocyanidins in Cranberries
- WG Initiative being planned for Cannabis

July 2016
- Form working groups to begin draft standard method performance requirements
- Ocean Spray became and AOAC Organizational Affiliate and supported the formation of a Working Group
- Six companies became AOAC Organizational Affiliates and Advisory Panel meeting held for Cannabis

July -August 2016
- Comment on draft standard method performance requirements
- Working Group chairs identified for both proanthocyanidins in cranberry products and for Cannabis potency.

September 2016
- SPDS to deliberate and reach consensus on a final versions of the standard method performance requirements
- WG chairs will present launch presentations and draft fitness for purpose statements for stakeholder deliberation and consensus.

AOAC Standard Method Performance Requirements (SMPRs)
- Published in *Official Methods of Analysis of AOAC INTERNATIONAL*
- Manuscript published in *Journal of AOAC INTERNATIONAL*

Stakeholder Panel Composition

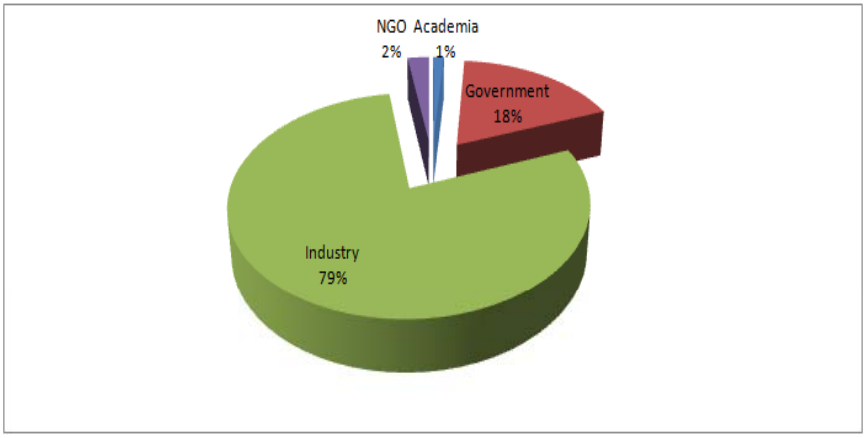
- Product Manufacturers
- Analyte/Method Subject Matter Experts
- Technology Providers
- Method Developers
- Government and Regulators
- Contract Research Organizations
- Reference Materials Developers
- Ingredient Manufacturers
- Method End Users
- Academia & Research
- Non Governmental Organizations
- Other as identified

Anyone with a material interest can participate
Balanced group of representative voting stakeholders
Chair and voting stakeholders vetted by AOAC Official Methods Board

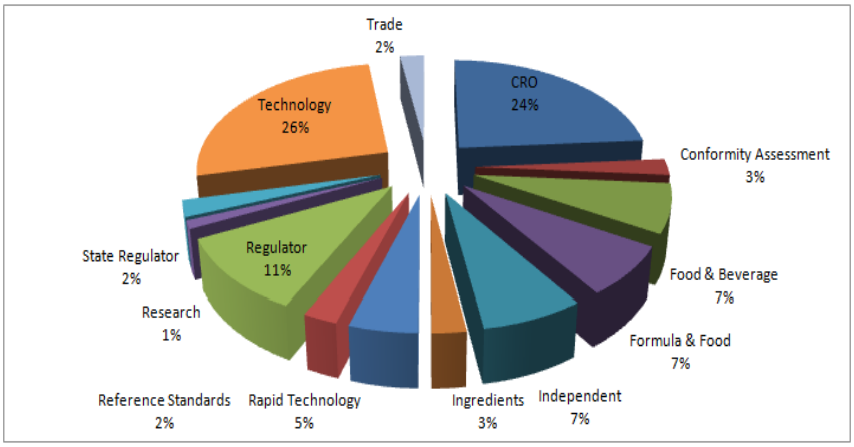
Organizational Meeting Registrants

Abbott Nutrition	Fonterra Cooperative Group Ltd.	Q Laboratories, Inc.
Advion Inc.	ImmunogenX	Retired
Agilent Technologies	Kombucha Brewers International	S. A. Audino & Associates
Alkemist Labs	Merieux NutriSciences	SC Labs
Archer Daniels Midland Company	MilliporeSigma	SCIEX
AsureQuality, New Zealand	National Food Agency	Shimadzu Scientific Instruments, Inc.
Canadian Food Inspection Agency	Neogen	SPEX SamplePrep
Certified Laboratories, Inc.	Nestle Research Center	The Coca-Cola Company
Covance Laboratories	NIST	Thermo Fisher Scientific
Crystal Diagnostics - NEOMED	Ocean Spray Cranberries	University of Saskatchewan
Curtis S. Phinney, CNS	Perrigo / PBM Nutritionals	US Alcohol & Tobacco Trade Bureau
Eurofins Central Analytical Laboratory	Phenomenex, Inc.	US FDA
First Source Laboratory Solutions LLP	PhytoLab GmbH & Co., KG	US Treasury (Retired)
Florida Department Of Agriculture And Consumer Services	Pickering Laboratories, Inc.	USDA
		Waters Corporation

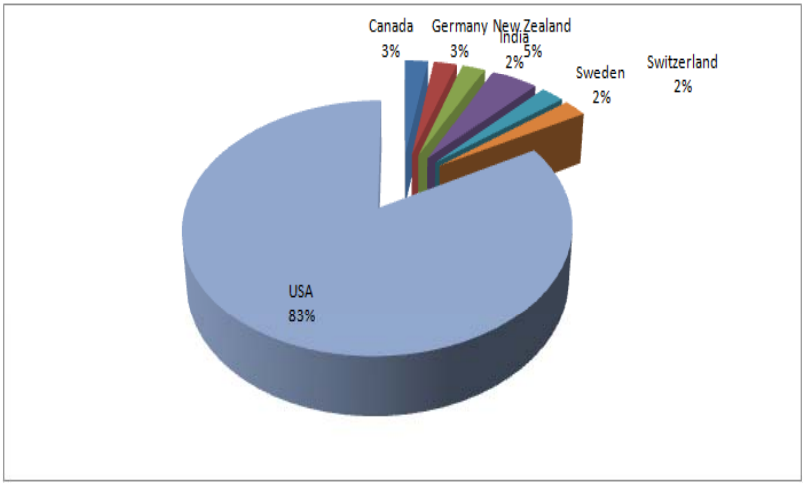
SPSFAM Registrants by Broad Perspectives



SPSFAM Registrants by Specific Perspectives



SPSFAM Registrants by Regions



Proposed SPSFAM Representative Voting Members

CFIA/University of Saskatchewan	Crystal Diagnostics (NEOMED) / Neogen
US TTB	SCIEX
National Food Agency	Thermo Fisher Scientific
Florida Dept. of Agriculture	SPEX SamplePrep
US FDA / USDA	MilliporeSigma
US NIST	Shimadzu Scientific / Waters Corporation
AsureQuality	Agilent
PhytoLab GmBH & Co., KG	Nestle
SC Labs	Merieux NutriSciences / Eurofins
Q Laboratories	S. A. Audino & Associates
Covance Laboratories / Alkemist Labs	Curtis S. Phinney, CNS
Ocean Spray Cranberries	Kombucha Brewers International
The Coca-Cola Company	
Abbott Nutrition / Fonterra Cooperative	
Archer Daniels Midland / Perrigo/PBM Nutrtionals	

alternates

Launching AOAC Stakeholder Panel Working Groups

- Working Group Chair or designee will present on the background, regulations, and analytical challenges of the priority. The WG chair will also propose a draft fitness for purpose statement that will serve as the basis for the working group's SMPR development.
- SPSFAM chair will entertain deliberation on the draft statement
- After due deliberation by ALL of the assembly, and potential tweaking, SPSFAM chair will call for an endorsement of the fitness for purpose statement
- Information will be available for attendees to sign up to participate on the working group

Documentation and Communication

- AOAC carefully documents the actions of the Stakeholder Panel and the Working groups
- AOAC will prepare summaries of the meetings
  - Communicate summaries to the stakeholders
  - Publish summaries in the *Referee* section of AOAC's *Inside Laboratory Management*
- AOAC publishes its voluntary consensus standard
  - *Official Methods of Analysis of AOAC INTERNATIONAL*
  - *Journal of AOAC INTERNATIONAL*
- AOAC publishes the status of standards in the *Referee* section of AOAC's *Inside Laboratory Management*

Roles and Responsibilities

- Stakeholder Panel
  - Establish working groups to develop standards
  - Comment, deliberate, and establish voluntary consensus standards
- Stakeholder Panel Working Groups
  - Develop draft standard method performance requirements
  - Reconcile comments
  - Present draft standard to stakeholders
- Official Method Board
  - Vet and approve stakeholder panel chair and representative voting stakeholders
  - Assign representative to serve as a resource to stakeholder panel
- AOAC Staff
  - Coordinate stakeholder panel, working groups, and facilitate their meetings
  - Document actions/decisions of working groups and stakeholder panel
  - Post SMPRs and collect comments for draft SMPRs

QUESTIONS?

THANK YOU

☺