AOAC Research Institute

A division of AOAC INTERNATIONAL

PERFORMANCE TESTED METHODS[SM] (PTM)

PROGRAM

POLICIES and PROCEDURES

Notice: AOAC Research Institute reserves the right to modify the program at any time. Participants are required to comply with the current program in effect at time of initial application or renewal.

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POLICIES and PROCEDURES

1. Purpose

The *Performance Tested Methods* (PTM) program provides an independent third-party review of proprietary test kit method performance. Test kit methods demonstrated to meet acceptable performance criteria are granted PTM status. Method Developers of approved PTM methods are licensed to use the PTM certification mark, which assures users that an independent assessment has found the method performance meets an appropriate standard for the claimed intended use.

2. Background

The AOAC Research Institute (AOAC RI) is a nonprofit division of AOAC INTERNATIONAL. The mission of the AOAC RI is to promote and provide technical support to activities related to the development, improvement, and validation of proprietary methods. A current list of PTM certified methods can be found at the AOAC RI website at: https://members.aoac.org/AOAC_Prod_Imis/AOAC/PTM_Validated_Methods.aspx.

The AOAC Research Institute cooperates with many US and international organizations including US Food and Drug Administration, US Department of Agriculture, US Department of Homeland Security, US Department of Defense, US Environmental Protection Agency, US National Atmospheric and Oceanic Administration, Canadian Food Inspection Agency, Health Canada, Association Française de Normalisation, Nordic Committee on Food Analysis, MicroVal, and the International Organization for Standardization.

The PTM program is designed to be complementary to the *Official Methods of Analysis*℠ (OMA) program. The PTM evaluation can serve as the OMA single laboratory validation study.

3. Overview

The PTM program has six distinct phases (see Figure 1):

1) AOAC RI Consulting (optional)
2) Submission of PTM Application
3) Method Developer Validation Study
4) Independent Laboratory Validation Study
5) Preparation of Method Validation Study Report
6) PTM Certification Review

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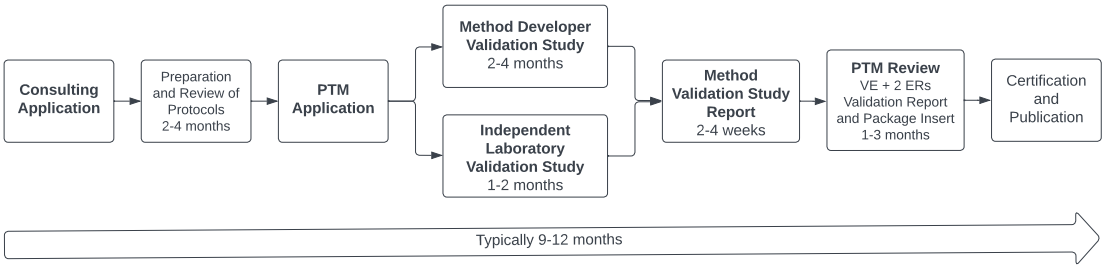

Figure 1. Timeline of PTM Process

AOAC RI Consulting

The initial phase of the PTM process begins with the development of a Validation Outline. In this phase, the Method Developer and an AOAC RI Technical Consultant discuss and decide the aims and scope of the validation. The assay type, target analyte(s), matrixes, market, and regulatory issues are all considered at this stage. The AOAC RI Technical Consultant works with the Method Developer to prepare a Validation Outline suitable to the claimed intended use of the method.

The Validation Outline is a formal document that includes a detailed description of the Method Developer and Independent Validation Study Protocols for data collection and statistical analysis with acceptable performance criteria. The Validation Outline is reviewed by the appropriate AOAC Volunteer Expert before formal method validation work begins. Once approved, the final outline is provided to the Method Developer and execution of each protocol can begin.

The Consulting service is optional, but highly recommended. Method Developers assume all risks for acceptability of self-generated study protocols. Data that do not comply with acceptable study designs may not be approved. Method Developers risk lengthened review time and additional testing expense due to errors in self-generated study protocols.

Submission of PTM Application

After the Consulting phase is complete and an approved Validation Outline has been delivered, the Method Developer may choose to submit a PTM Application. Method Developers are under no obligation to submit a PTM Application if they elect not to proceed.

A Method Developer who decides to proceed must submit a PTM application package as per section 4.2 before the Independent Laboratory Study can begin. The AOAC RI Senior Manager reviews the application package to confirm that the package is complete and assigns an AOAC RI Technical Consultant to lead the evaluation. Typically, this is the same Technical Consultant from the Consulting phase.

Method Developer Validation Study

The Method Developer may begin data collection according to the Method Developer Study Protocol from the Validation Outline at any time after the consulting phase is completed and the method validation plan has been approved.

Independent Laboratory Validation Study

After the PTM application has been submitted, the Technical Consultant and Method Developer identify qualified Independent Laboratories from the current list of Approved Independent Laboratories found on the AOAC RI Resources webpage to conduct the Independent Laboratory Study as detailed in the Validation Outline. It is the responsibility of the Method Developer to negotiate a financial agreement with the selected Independent Laboratory to conduct the study.

Once the Independent Laboratory Study is ready to begin (test kits have been delivered and Independent Laboratory has been trained), the Technical Consultant oversees the study. This oversight is conducted in the absence of direct communication between the Method Developer and the Independent Laboratory as per the specifications of the AOAC Independent Laboratory Agreement on file for the laboratory.

Upon completion of Independent Laboratory testing, a written Independent Validation Study Report is completed and submitted to the AOAC RI Technical Consultant. After review to ensure completeness and adherence to the protocol requirements, the AOAC RI Technical Consultant delivers the report to the Method Developer.

Preparation of Method Validation Study Report

The Method Developer shall prepare a PTM Validation Study Report per the current PTM study report format provided by the Technical Consultant. The completed report includes the results from the Method Developer Validation Study and the Independent Laboratory Validation Study.

PTM Certification Review

The Technical Consultant shall choose 2 Expert Reviewers from the AOAC RI list of Approved Vetted Experts. The AOAC Volunteer Expert and 2 Expert Reviewers review the Method Validation Study Report and the test kit package insert to determine acceptability as a *Performance Tested Method*. The Reviewers provide recommendations to the Technical Consultant for awarding or denying PTM status.

PTM Certification is granted if there is consensus of the AOAC Volunteer Expert and 2 Expert Reviewers that the performance of the method is acceptable relative to the Validation Outline criteria and appropriate standard [reference method, guideline, and/or AOAC *Standard Method Performance Requirements* (SMPRs®) when available] for the method's intended use claim. Once approved, the method is awarded a unique PTM certification number. The Method Developer is licensed to use the PTM certification mark, and the pertinent validation study data are published within the PTM certificate on the AOAC website.

PTM status is extended in one-year increments and must be renewed annually for as

long as the Licensee elects to maintain the PTM certificate.

4. Procedures

4.1 AOAC RI Consulting Service (Optional)

Method Developers seeking PTM status for a test kit method may use the AOAC RI Consulting Service. The AOAC RI maintains a pool of Technical Consultants with expertise in PTM program procedures and technical requirements. The AOAC RI Senior Director or Senior Manager will assign a Technical Consultant when a Consulting Application is submitted.

The Method Developer may request a specific Technical Consultant for their validation project(s). Requests will be honored whenever possible. However, the Senior Director shall have the ultimate decision as to which Technical Consultant is assigned to a project.

Consulting Service fees vary. See the current AOAC RI Fee Schedule posted on the RI webpage for details. AOAC RI Contributing Members are eligible for discounted consulting fees.

4.1.1 Consulting Application Package

A Method Developer requesting Consulting Services must submit:

1) Consulting Application (see AOAC RI Webpage)
2) Copy of the test kit package insert and/or or user manual.

Applications are submitted through the AOAC RI webpage.

4.1.2 Validation Outline

The purpose of the consulting service is to clearly define the intended use claims for which a Method Developer seeks PTM status, and to deliver a Validation Outline that allows the Method Developer and Independent Laboratory to validate those claims as efficiently as possible. The Technical Consultant will communicate with the Method Developer by email, telephone, or virtual meeting to discuss the goals and scope. The Technical Consultant will produce a draft Validation Outline after this initial communication.

The Validation Outline includes:

1) A statement of principle of the method and intended use claim
2) Matrixes to be tested to support intended use claim
3) Method Developer Validation Study Protocols

4) Independent Laboratory Validation Study Protocols
5) Statistical analyses required
6) Appropriate reference method(s) and/or reference materials with acceptance criteria or a relevant SMPR.
7) Validation Study Report Template

The Validation Outline is reviewed and approved by the appropriate AOAC Volunteer Expert.

Study Protocols approved by the AOAC Volunteer Expert **are binding** and may not be altered or revised *ex post facto* by the Method Developer, the Expert Reviewers, or the AOAC Volunteer Expert except by consensus of all parties.

An approved Validation Outline is considered expired one year after approval and will require re-review and approval with any appropriate revisions by the AOAC Volunteer Expert if no work has been started within a year of initial approval.

4.1.3 Payment and Delivery of the Validation Outline

AOAC INTERNATIONAL will issue an invoice for the Consulting Service when the Consulting Application package is received by the AOAC Research Institute. The invoice will be on a NET 30-day term from the date of the invoice.

The final approved Validation Outline **will not** be delivered to the Method Developer until the consulting fees are received. A consulting project shall be considered completed when the Validation Outline with approval by the appropriate AOAC Volunteer Expert is delivered to the Method Developer.

4.2 *Performance Tested Methods* Application

Method Developers seeking PTM status for test kit methods must submit a PTM application package for **each** method to be evaluated prior to the Independent Laboratory Validation Study. The *Performance Tested Methods* Application form is available on and submitted via the AOAC RI webpage.

A PTM application package must contain the following:

1) Completed *Performance Tested Methods* Application Form
2) Test kit package insert(s), labels, and operator's manual(s)
3) Manufacturing Quality Assurance program description or a copy of the International Organization for Standardization (ISO) 9001:2015, 13458:2016, and/or cGMP certificate where applicable for proprietary

test kits and instruments.

Method Developers may recommend potential Expert Reviewers. However, AOAC RI is not obligated to accept the recommendations of the Method Developer. Expert Reviewers must meet the requirements in Section 10.2.4.

Methods that have been previously certified by comparable method validation organizations may be applicable for PTM status. Method Developers interested in obtaining PTM status may submit a *Performance Tested Methods* application package. Method Validation Study Reports must be in the current PTM report format and include appropriate AOAC statistical analyses of data prior to the review process.

4.2.1 *Performance Tested Methods* Application Review

The PTM Application package will be reviewed for completeness by AOAC RI staff. An email will be sent to the Method Developer if required information is missing. An invoice will be sent to the Method Developer within five business days of receiving an application.

4.2.2 Documentation of QA Program and QC Practices

Method Developers must submit a description of the quality assurance program and quality control practices used in the manufacturing, production, storage, and delivery of the test kit, its components, and/or instrumentation. The description must include the sampling system followed with particular reference to the tests used to verify that test kit production meets established production standards. To protect proprietary information, the description may be submitted in the form of a signed letter with no more than a four- to six- page description of the QA/QC program. **Note**: test kits used in the validation studies must be final GMP manufactured products. Research and development test kits and components cannot be used.

The Method Developer shall use a performance monitoring system that will provide production management with the information necessary to assure that the test kit components continue to meet the requirements of the specifications to which the test kit was originally evaluated and granted PTM status. The system shall include the methods, procedures, controls, records, and maintenance of the system to provide continuing assurance of compliance with the performance specifications advertised. The extent of this system will depend on the characteristics of the test kit method and on the performance specifications. In lieu of a description of QA/QC practices, the Method Developer may submit a copy of the ISO 9001:2015, ISO 13458:2016, or cGMP certificate that applies to the manufacturing site.

4.2.3 Technical Consultant

A Technical Consultant is assigned by the AOAC RI Senior Manager when a PTM application is received. Typically, the Technical Consultant who provided the Consulting Service, if applicable, is assigned for the PTM review. A Method Developer may request a different Technical Consultant at any time by contacting the AOAC RI Senior Manager.

4.2.4 Invoicing

AOAC INTERNATIONAL will issue an invoice for the PTM application when notified by the AOAC RI that an application package has been received. Payment is required on a NET 30-day term from the date of the invoice.

4.3 Method Developer Validation Study

Method Developers are responsible for collecting data for the Method Developer Validation Study. The study should conform exactly to the Method Developer Validation Protocol in the Validation Outline developed during the consulting phase. Any question(s) or proposed deviation(s) from the Method Developer Validation Study Protocol must be submitted to the Technical Consultant before data collection begins. The Technical Consultant will confer with the AOAC Volunteer Expert regarding the question(s) or proposed deviation(s) and report back to the Method Developer.

Method Developers may collect Method Developer Validation Study data at their own facilities, or the Method Developer Validation Study may be contracted to a contract laboratory of the Method Developer's choice. Results from the Method Developer Validation Study must be included in the Method Validation Study Report.

If the Method Developer elects to assign all matrix testing to the Independent Laboratory during the consulting phase, the Method Developer is not required to provide any matrix testing data.

4.4 Independent Laboratory Validation Study

The Method Developer may choose to request proposals from more than one Independent Laboratory. Factors in the selection of an Independent Laboratory can include cost, timing, technical expertise, and ease of shipping method components and equipment. Independent Laboratories shall be selected from the current list of AOAC RI approved Independent Laboratories on the AOAC RI webpage and the Method Developer must notify the Technical Consultant of their selection. The Technical Consultant may assist the Method Developer in

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the Independent Laboratory selection process. The Method Developer enters into a financial agreement with the chosen laboratory for performance of the Independent Laboratory study.

4.4.1 Test Kit Method Evaluation

A laboratory cannot be selected to evaluate a particular test kit method if that laboratory routinely uses the method under evaluation or has participated in the development of the method. Also, the Independent Laboratory must not have a financial, corporate, or regulatory relationship with the applicant and must not be a competitor.

4.4.2 On-site Validation

A method that requires large and/or expensive equipment not available and not easily installed at an Independent Laboratory may be evaluated *in situ* at the Method Developer laboratory with the following additional requirements:

1) Validation materials and test portions must be prepared and blind-coded by an AOAC RI Approved Independent Laboratory.
2) A separate analyst from the Independent Laboratory must analyze the blind-coded test samples at the Method Developer laboratory without influence from Method Developer personnel.
3) An AOAC RI Technical Consultant must be present during the analysis.
4) Results must be reported back to the Independent Laboratory.
5) The Independent Laboratory will decode and analyze the data and prepare a report.

4.4.3 Logistics, Training, and Conduct of Study

It is the responsibility of the Method Developer to ensure that all materials needed for the Independent Validation Study are delivered to the Independent Laboratory and that training of the Independent Laboratory on performance of the candidate method is carried out if requested.

It is the responsibility of the Independent Laboratory to perform the Independent Validation Study according to the approved Independent Validation Study Protocol. Once the study is initiated, all communication about the study protocol or the method under review must be directed to the Technical Consultant, who may relay the question to the Method Developer or AOAC Volunteer Expert and then answer back to the Independent Laboratory. The Technical Consultant may choose to call a

group conference call between the Independent Laboratory and the Method Developer if the questions are particularly difficult, or if the Technical Consultant feels that the flow of information needs to be improved.

However, in ALL cases, the Technical Consultant will facilitate and be present during any communication between the Independent Laboratory and the Method Developer, and NO communication shall occur between the Method Developer and the Independent Laboratory without inclusion of the Technical Consultant while the study is in process.

In some cases, additional testing is required to complete a project. If additional testing is required, the Independent Laboratory must provide the Technical Consultant with a cost estimate for the additional work. After conferring with the Method Developer, the Technical Consultant shall approve or decline the additional work.

4.4.4 Independent Validation Study Report

Data will be reported in the format specified in the Independent Validation Study Protocol, which may require the calculation of statistics as defined in the protocol for each matrix evaluated. All Independent Laboratory data will be reported directly to the AOAC RI Technical Consultant. The Technical Consultant will review the Independent Validation Study Report for completeness, detail, adherence to the Independent Validation Study Protocol, and proper application of statistical tools. Once any revisions are made, the report is sent to the Method Developer.

4.5 Method Validation Study Report and Review

Method Developers are required to prepare and submit a Method Validation Study Report supporting the intended use claims of the method according to the current PTM Report Format supplied by the Technical Consultant. The Method Validation Study Report must include the results of the Method Developer Validation Study and the Independent Validation Study, including all original and retest data.

The current draft package insert and/or user manual is reviewed at the same time as the Method Validation Study Report to ensure that the package insert and/or user manual is complete, accurate, and consistent with the Method Validation Study Report. The basic requirements for package inserts are outlined in the Appendix.

The Method Validation Study Report and draft package insert and/or user

manual shall be submitted directly to the Technical Consultant, who will forward the documents with the appropriate review form to the AOAC Volunteer Expert and two Expert Reviewers. It is the responsibility of the Technical Consultant to set deadlines during the review process and track progress of the reviews. Generally, reviewers are asked to provide comments and questions within 2 weeks for the first review and 1 week for each review thereafter.

Upon receipt of all review forms, the Technical Consultant shall compile a list of recommendations and comments with blinding of Reviewers 1, 2, and 3, and forward the compiled comments to the Method Developer. The Method Developer is responsible for responding to all reviewer comments and questions in writing. All responses and revised documents shall be submitted to the Technical Consultant, who will forward them to the AOAC Volunteer Expert and Expert Reviewers for additional comment or approval. The process continues until consensus is reached among the three reviewers for either approval or rejection.

4.6 Selecting Reviewers

For each application for PTM status, at least 2 Expert Reviewers and 1 AOAC Volunteer Expert will be assigned to review the Method Validation Study Report and package insert or user manual. The AOAC RI Technical Consultant is responsible for recruiting 2 Expert Reviewers from the list of AOAC RI approved trained Expert Reviewers and identifying the appropriate AOAC Volunteer Expert.

Method Developers may recommend individuals as Expert Reviewers (see requirements in 10.2.4); however, the final assignment will be at the sole discretion of the AOAC RI Technical Consultant. The experts selected to evaluate specific test kit methods must not have a relationship (including as a financial investor, member of board of directors, or consultant) with the applicant, be competitors or closely related parties, nor have any business relationship other than as a customer.

If there is no AOAC Volunteer Expert for a particular topic area, every effort should be made to recruit an AOAC RI method volunteer who is a member of a relevant Expert Review Panel to serve as an AOAC Volunteer Expert. If a relevant Expert Review Panel does not exist, then the *Official Methods* Board (OMB) will be consulted for recommendations for an AOAC Volunteer Expert.

4.7 Criteria for Granting *Performance Tested Methods* Status

The AOAC Volunteer Expert and Expert Reviewers, acting as independent reviewers, decide whether the results documented in the Method Validation Study Report merit awarding PTM status.

The reviewers must be satisfied that results from the Method Developer and Independent Validation Studies provide a solid scientific case for granting PTM status. The criteria for granting PTM status are based on:

1) Results from the Method Developer and Independent Validation Studies combined support and confirm all claims made in the test kit method's package insert and/or user manual.
2) All results support a conclusion that the candidate method meets the performance requirements of the relevant guideline and/or AOAC *Standard Method Performance Requirements* for the matrixes and analytes claimed.
3) Results support the consistent manufacturing and claimed shelf life of the test kit.

In some rare cases if an impasse develops between the Method Developer and a reviewer, it is the responsibility of the Senior Director of the AOAC RI to facilitate a resolution. If a resolution cannot be reached, the Senior Director of the AOAC RI may convene a special meeting to resolve all remaining questions.

4.8 PTM Certificate

A PTM certificate is issued by the AOAC RI to the Method Developer for each test kit method granted PTM status. The certificate carries a unique certification number, name of the approved test kit method, key data from the validation study, and a log of approved method modifications. PTM certificates are publicly available in a searchable database on the AOAC RI webpage.

4.8.1 Certificates Initially Granted Before October 1st of Any Given Year

The initial PTM certificate is granted and effective for a term expiring on December 31st of the same year.

4.8.2 Certificates Initially Granted on or After October 1st of Any Given Year

The initial PTM certificate is granted for a term expiring on December 31st of the **next** year.

4.9 PTM Certification Mark

Method Developers of approved methods are licensed to use the PTM certification mark on their packaging and promotional materials (see Figure 1). Use of the certification mark is entirely optional but highly encouraged. Method Developers will receive a copy of the certification mark with a unique certification number as soon as the test kit method is PTM approved.

Figure 1. PTM Certification Mark

4.10 Certification Mark License Agreement

A Certification Mark License Agreement between the AOAC RI and the Method Developer must be signed before the certification mark can be used. The License Agreement describes the rights, obligations, rules, and procedures in the use of the PTM certification mark. A single agreement may be used to cover all PTM approved test methods in cases where a Method Developer owns more than one method awarded PTM status.

A Method Developer company officer must sign the License Agreement to use the PTM certification mark. Method Developers are not required to sign the License Agreement until the PTM review is complete and the candidate method is granted PTM status. **Method Developers are encouraged to review the License Agreement before submitting a PTM Review Application to the AOAC Research Institute**.

Distributors of the Method Developer's certified test kit(s) are required to sign an Addendum to the License Agreement to indicate they will adhere to the rights, obligations, rules, and procedures in the use of the PTM certification mark.

5. *Performance Tested Methods* Status

5.1 Publication

The Method Validation Study Report approved by the Reviewers in awarding PTM status can be submitted for publication in the *Journal of the AOAC INTERNATIONAL (JAOAC)*. Submissions are made directly to JAOAC via the online submission site. AOAC staff and the Technical Consultant provide instructions for submission.

5.2 *Inside Laboratory Management*

The Method Developer may prepare and submit an article for the AOAC magazine *Inside Laboratory Management* (ILM). The ILM article should be about 1 – 2 magazine pages in length. The ILM article should be submitted to the ILM editor.

5.3 Database of Certified Methods

The AOAC RI will maintain and publish a regularly updated searchable database of current certified methods on the AOAC website.

6. Annual Renewal Process

The AOAC RI Senior Manager and the certification Technical Consultant are responsible for conducting the Annual Renewal process. PTM status is granted in periods of one calendar year after the initial certification.

Each PTM certificate expires on December 31st unless otherwise indicated. Annual renewal notifications and invoices are distributed in September. An Annual Renewal Application and an Annual Renewal Fee must be submitted to the AOAC RI by the Licensee for each expiring *Performance Tested Method* certificate by December 1st. Application submission is made online through the AOAC RI webpage.

Renewal fees for the 1st year following certification will be pro-rated based on the month the method is certified, through the end of September. For example, a method that is approved for certification on June 1, will be invoiced for ½ of the full annual renewal fee. Methods that are certified in October through December are given an expiration date of December 31 of the following year.

The AOAC RI will endeavor, to the best of its ability, to provide Licensees with timely notice of the pending certificate expiration by email. **It is the responsibility of the Licensee to provide the AOAC Research Institute with changes in contact information.** Ultimately, it is the responsibility of the Licensee to submit an Annual Renewal Application and Fee for each *Performance Tested Method* the Licensee intends to keep in good standing.

The purpose of the Annual Renewal is to affirm that no changes have been made to the test kit method since the last review or renewal and to confirm that the method performs as most recently evaluated; or to review any modifications to the test kit method components, instrumentation, intended use claims, or package insert. Modifications to any of these parameters may require additional data.

The test kit method will be granted a one-year certificate if the Licensee certifies that no changes have been made to the test kit method since the previous renewal or review and that the method performs as most recently evaluated; or that sufficient data are provided demonstrating that the method performs as well or better than the most recently reviewed version if any changes have been made to method components,

instrumentation, intended use claims, or package insert.

A new or supplemental QA/QC package must be submitted with the Renewal Application if changes have been made in the manufacturing or QC testing processes. The AOAC RI reserves the right to request and review QA/QC records to verify that the consistency of test method performance is maintained throughout the life of the test kit method.

6.1 Late Fees

The deadline for annual renewal submissions and fee payments is December 1st. Expiring certificates not renewed in full (renewal application and fee) by December 31st are subject to a late fee per the Fee Schedule posted on the AOAC RI website. Thereafter, an additional monthly fee per certificate will be assessed for certificates not fully renewed by January 31st.

6.2 Modifications Submitted with Annual Renewal

If modifications to a previously PTM Certified method are planned, Method Developers must contact the AOAC RI to determine the associated Modification Level (see Modification Guideline on the AOAC RI website) and data requirements to support the modification, if any. The AOAC RI will consult with the AOAC Volunteer Expert for any clarifications.

Level 1 - Method modifications of this level may be submitted with the Annual Renewal documentation for review at no additional charge to the Method Developer.

Level 2 or 3 – Method modifications that are determined to be either Level 2 or Level 3 are assessed a Level 2 or 3 modification fee (see Fee Schedule on the AOAC RI Resources webpage) and **must be submitted separately from renewals** using the modification application on the AOAC RI website.

6.3 Suspension of Certification

PTM status shall be suspended if:

1) Serious adverse comments with supporting data have been received from method users indicating the method does not consistently perform as claimed, and the Method Developer has not provided a satisfactory resolution.
2) Undisclosed modifications are discovered for which the Method Developer did not submit data, or the data submitted in support of modifications is determined to be insufficient to demonstrate comparable or better performance relative to the original condition of PTM approval (see section 6).

3) An Annual Renewal Application, renewal fee, and late fee have not been received by January 30. Suspension will begin on February 1.

Suspended methods will be removed from the database of certified methods maintained by the AOAC Research Institute on the AOAC website, and the Licensee may not claim that the method is certified as a *Performance Tested Method*.

6.4 Re-Instatement of Suspended Methods

Licensees may seek reinstatement of a suspended *Performance Tested Method* for a period of up to six months after the renewal due date by submitting an Annual Renewal Application, Annual Renewal fee, all applicable late fees, plus any additional data and/or information addressing the serious adverse complaints or undisclosed modifications.

6.5 Revocation

The AOAC RI, at its sole discretion, may revoke PTM status and cancel any license for the use of the certification mark at any time for any of the following reasons:

1) The PTM status of a method has been suspended for 6 months for any reason.
2) The Licensee has not complied with the original agreement relative to use of the Research Institute's certification mark.
3) The Licensee has not responded adequately or has not taken timely corrective action relative to poor performance of the method as reported by method users or others.
4) The Licensee modified the certified method in a manner that could reasonably be expected to affect its performance characteristics and failed to notify the AOAC RI.
5) The Licensee requested that PTM status be discontinued.
6) The PTM program requirements changed and the Licensee either did not or cannot ensure conformance to the new requirements within a reasonable amount of time. The Licensee will be allowed up to 60 days, but not later than the expiration of the current certificate, to comply with any new program requirements.
7) The Licensee ceased to produce the test kit method.
8) The Licensee failed to meet financial obligations to the AOAC RI.

When the PTM status of a method is revoked, the PTM certification mark must be removed from all packaging and promotional literature. The Method Developer and its distributors must cease any claims as a *Performance Tested Method*.

6.6 Re-Instatement of Revoked Methods

Revoked *Performance Tested Methods* may be submitted for Re-Instatement if no changes have been made to the method and **no** serious adverse comments have been received.

The Method Developer must collect data (at a new production location if applicable) that compares the performance of the test kit to the appropriate standard (reference method(s), guidelines, and/or SMPRs) where applicable.

Method comparison data for each reference method must be submitted if more than one reference method was examined in the original validation study and at least 3 total matrices unless fewer are claimed. The Method Developer must submit a formal report containing the results of the method comparison study and any other data deemed necessary by the AOAC RI in consultation with the Volunteer Expert to address prior complaints or issues. The new data collected for re-instatement must demonstrate that the method performs as well or better than the original data.

If approved for re-instatement, the method will be certified until the end of the calendar year. Renewal fees for the 1st year following recertification will be pro-rated based on the month the method is recertified, through the end of August. For example, a method that is approved for re-certification on June 1, will be invoiced for ½ of the full annual renewal fee. Methods that are recertified in September through December are given an expiration date of December 31 of the following year.

Thereafter, annual renewal fees will be assessed in full every year as long as the Method Developer desires to maintain the PTM status for the test method (assuming the Method Developer and the method comply with all AOAC RI policies and procedures.)

7. Method Modifications

7.1 Notification

It is the responsibility of the Licensee to notify the AOAC RI when changes are made to the method that affect in any way (1) the instructions for using the method; (2) the method's performance; (3) the manufacture of the method components; or (4) the applicability of the method. **Failure to appropriately notify the AOAC Research Institute of changes may result in revocation of the PTM certification**.

Licensees are contractually obligated to provide the AOAC RI documentation of changes made in a certified PTM method. The AOAC RI, generally in consultation with appropriate experts, will determine the level of modification and the data

required to support the change. The licensee must submit a Method Modification Application with the corresponding fee.

7.2 Modification Review Levels and Administrative Fees

A Method Modification Application describing the modification must be submitted and the AOAC RI must approve the modification **before** a Licensee may use the certification mark on a modified method. Applications are made online from the AOAC RI webpage.

Administrative fees to review modifications to test kit methods are based on the amount of resources required on the part of the AOAC RI and its Reviewers to evaluate the changes (see Fee Schedule on the AOAC RI webpage). Modification of a validated *Performance Tested Method* may require a Level 1, Level 2, or Level 3 Review depending on the change to the validated method.

In general,

- Level 1 modifications require little to no data and an internal AOAC RI review;
- Level 2 modifications require limited data and either internal or AOAC Volunteer Expert review; and
- Level 3 modifications require extensive data and a full review (AOAC Volunteer Expert plus 2 Expert Reviewers).

Refer to the current Modification Guideline (available on the AOAC RI website) for a detailed description of modification levels and supporting data requirements.

The Licensee must submit a copy of the package insert, plus all appropriate data. An exact determination of the level of the modification can only be made by the AOAC RI after a written explanation and a completed application are received and reviewed by the AOAC RI. Modification Levels will be determined by the AOAC RI with the assistance of the appropriate AOAC Volunteer Expert.

7.3 Identical Multiple Modifications

Identical Level 1 or Level 2 modifications to a series of related methods sharing a common platform may be submitted as one Modification Application. For example, if a Licensee has three PTM certified test kits: one for *Salmonella*, one for *Listeria* genus, and one for *E. coli* and all are based on PCR using the same thermal cycler platform and reagents, the Licensee may submit one Method Modification Application that applies to all three if the same Level 1 or Level 2 modification applies to all three methods. For example, the Method Developer

may choose to modify the same liquid reagent to a lyophilized reagent in each of the kits. The Licensee will be assessed a Modification Review fee (appropriate to the modification level) for the first three methods in the group modification according to the Fee Schedule on the AOAC RI website.

The Licensee must submit a single Method Modification Application and all supporting documents at the same time.

Licensees should contact the AOAC RI to determine the modification level and if the modifications can be considered identical. The AOAC RI will consult with the AOAC Volunteer Expert to determine the modification level and applicability of this policy.

7.4 Approval of Modifications

Licensees will be notified in writing when their modification(s) are approved. The AOAC RI website database of Validated Methods will be updated to reflect any new claims and the PTM certificate will be updated to document the modification and, in some cases, supporting data will be added.

8. Complaints

8.1 Licensee Complaints

Formal Licensee complaints must be in writing and directed to the AOAC RI Senior Director. The AOAC RI Senior Director will initiate appropriate action to resolve the complaint.

8.2 User Complaints

Test kit method user complaints must be in writing and should be directed to the AOAC RI Senior Director. Complaints directed to the AOAC RI Senior Director will be forwarded to the Licensee for resolution**. Failure to adequately address user complaints will result in the AOAC RI initiating an inquiry and could lead to revocation of the method's PTM status**.

9. Appeals Process

9.1 Right to and Basis for Appeal

Method Developers who have submitted a PTM Application may appeal certain **final** decisions of the AOAC RI. The appeals process is not open to parties that have not submitted methods to the AOAC RI PTM Program nor to those seeking to appeal AOAC RI decisions regarding methods submitted by other Method Developers.

Appellants must comply with all relevant AOAC RI administrative procedures necessary to obtain an AOAC RI **final** decision before a formal appeal can be made to the AOAC RI.

Appellants may appeal an AOAC RI decision to 1) refuse acceptance of a PTM Application; 2) deny PTM status; 3) revoke PTM status; or 4) refuse renewal of PTM status. Appellants may appeal such final decision(s) of the AOAC RI based on alleged scientific or procedural error. Failure to agree on a testing protocol or the lapse of a certificate is not subject to appeal.

All decisions of the AOAC RI with regard to the action under appeal shall be stayed until the completion of the appeals process described herein.

9.2 Appeal Application

The appellant shall submit their appeal in writing within 30 calendar days after the date of notification of the **final** action being appealed. All appeals must be delivered by registered mail to:

Senior Director
AOAC Research Institute
2275 Research Blvd.; Suite 300
Rockville, Maryland 20850
United States of America

All appeals must include a U.S. one thousand-dollar (US$1000) deposit which will be deposited in an identifiable internal account by the AOAC RI. The deposit will be returned to the appellant or applied to the expenses of conducting the appeal, pending the outcome of the appeal (see section 9.7).

All appeals must be written in English and must include statements or materials regarding:

1) The **specific** decision being appealed,
2) The **specific** nature of the objection(s) to the decision, including any adverse effects,
3) The basis for the appeal, including the section(s) of the procedure(s) and/or protocol(s) and/or evaluation(s) that are at issue and data and other evidence in support of the appeal. Note: New data or evidence which was not made available to the AOAC RI and its Reviewers prior to reaching the decision under appeal **will not** be considered.
4) The **specific** remedial action(s) that would satisfy the appellant's objection(s),
5) All previous efforts to resolve the objection(s) and the results of each effort, and
6) A list of at least five appeals panel nominees who qualify under the

conditions of section 9.3 and are acceptable to the appellant.

Upon receipt, the AOAC RI Senior Director will immediately forward a copy of the Appeal to the Chair of the Official Methods Board (OMB).

9.3 Appeals Panel

The Chair of the OMB (or OMB designee) will determine whether the appeal is complete and acceptable within the requirements of section 9.2. If the Chair (or designee) determines the appeal to be incomplete or unacceptable, the appeal will be returned to the appellant with instructions on how to correct the deficiencies.

If the OMB Chair (or OMB designee) finds the appeal acceptable, the Chair will appoint an Appeals Panel of three persons within 30 calendar days of the date the appeal is received at the AOAC Research Institute. The Chair will appoint one member of the Appeals Panel to serve as the Appeals Panel Chair. At least two members of the Panel must be acceptable to the appellant and at least two members must be acceptable to the Senior Director of the AOAC RI.

The Appeals Panel shall consist of three individuals who have not been directly involved in the matter under appeal, who will not be materially or directly affected by any decision made by the Appeals Panel, and, generally, who possess expertise in the scientific area(s) which are the subject of the appeal. All Appeals Panel members shall be required to execute an agreement to adhere to the AOAC RI's "Trade Secret Non-disclosure Policy", "Conflict of Interest Policy", and "Anti-Trust Policy". These Policies are available from the AOAC RI Senior Director or Senior Manager.

9.4 Appeals Process

Appeals may be conducted by telephone, by written or electronic correspondence, or by video conferencing at the discretion of the Appeals Panel in consultation with the parties.

The appellant has the burden of demonstrating AOAC RI errors, AOAC RI unreasonable or arbitrary actions or inactions, and the appropriateness of the remedial action requested. The AOAC RI Senior Director has the burden of demonstrating that the AOAC RI took all actions in compliance with its policies and procedures; that the decision reached by the AOAC RI was reasonable, and where applicable, substantiated by scientific facts and data; and/or that the proposed remedial action requested by the appellant would be inappropriate.

The AOAC RI Senior Director shall prepare and submit a written response to the appeal to the Appeals Panel Chairman and appellant within 30 calendar days from the date the appeal is received at AOAC RI headquarters. The Appeals

Panel will review all pertinent information and, if necessary, may conduct an oral hearing by either telephone or virtual conferencing or an in-person meeting of the parties.

9.5 Preliminary Finding

The Appeals Panel shall produce a preliminary report within 30 calendar days of being formed or of receiving the AOAC RI's response to the appeal, whichever is later. The preliminary report shall contain the Appeals Panel's preliminary finding, and an explanation of the preliminary findings. The appellant and the AOAC RI shall have 14 calendar days to submit a response to the preliminary report to the Appeals Panel Chair.

9.6 Final Decision

The Appeals Panel shall make a final decision, by simple majority vote, within 14 calendar days of receiving the responses to the preliminary report. Within an additional 14 calendar days of announcing this final decision, the Chair of the Appeals Panel shall issue a final written report. The final report shall include 1) the original appeal, 2) the AOAC RI's response to the appeal, 3) the Appeals Panel's preliminary findings and explanations, 4) the appellant's and the AOAC RI's responses to the preliminary report, and 5) the Appeals Panel's final decision.

If the Appeals Panel finds for the appellant, the final report shall remand the action to the AOAC RI with specific findings and opinions of the facts and circumstances that demonstrate an incorrect decision was reached or an unreasonable or arbitrary action was taken **and with instructions to implement specific remedial action(s)**.

If the Appeals Panel finds for the AOAC RI, the final report shall contain specific findings and opinions of the facts and circumstances that demonstrate the AOAC RI acted properly and/or reached a reasonable decision based on the information available to it.

The decision of the Appeals Panel shall be final and non-appealable.

9.7 Expenses

If the Appeals Panel finds in favor of the appellant, the entire amount of the $1000 deposit shall be promptly returned to the appellant. If the Appeals Panel finds in favor of the AOAC RI, the $1000 deposit shall be applied to the expenses associated with the conduct of the appeal including the cost of any investigations, hearings and/or meetings conducted by the Appeals Panel.

9.8 Exceptions to the Procedures

The Appeals Panel may grant to itself and the parties, at its sole discretion, reasonable extensions of deadlines specified in these procedures. The Appeals Panel must notify, in a timely manner each of the parties.

The Appeals Panel serves at the pleasure of the Chair of the OMB. Any or all members of the Appeals Panel may be removed and replaced for failure to act in a timely or professional manner.

10. Program Administration

10.1 AOAC Research Institute

The PTM program is operated by the AOAC RI, a division of AOAC INTERNATIONAL, a nonprofit organization organized under the laws of the State of Maryland.

10.2 Responsibilities

The AOAC RI staff consists of a Senior Director, Senior Manager, Technical Consultants, and administrative support. AOAC RI Reviewers consist of AOAC Volunteer Experts and Expert Reviewers. AOAC RI Independent Laboratories consist of laboratories that have been trained and approved to carry out validation studies.

10.2.1 Senior Director Responsibilities:

1) Financial oversight of the program as a whole and all decisions pertaining to product and services fees.
2) Maintenance of and revisions to the Program Policies and Procedures.
3) Enforcement of policies and procedures.
4) Strategic planning.
5) All personnel decisions.
6) Oversight of the issuance of PTM certificates.

10.2.2 Senior Manager Responsibilities:

1) Provide application materials and assistance to potential Method Developers.
2) Conduct a preliminary review of the application materials for completeness of the package.
3) Establish and maintain a log and tracking system for all applications.
4) Assign projects to Technical Consultants.
5) Coordinate with AOAC Customer Service and Accounting

departments to ensure timely invoicing and collection of fees.
6) Manage annual certificate renewal process.
7) Maintain database(s) of applications and certified methods.
8) Provide status reports as appropriate.

10.2.3 Technical Consultant Responsibilities:

1) Develop Validation Study Protocols and coordinate reviews by the appropriate AOAC Volunteer Expert.
2) Assign Expert Reviewers to specific PTM applications.
3) Resolve situations where the original reviewers do not agree on the recommendation.
4) Qualify Independent Laboratories and monitor their work.
5) Coordinate and expedite the PTM process with Method Developers, Independent Laboratories, and Expert Reviewers.
6) Complete and issue required forms and reports.
7) Update and present the Method Validation Training Course in public and private forums throughout the year.
8) Maintain a pool of qualified trained Expert Reviewers and designated Volunteer Experts.
9) Maintain a pool of qualified trained Independent Laboratories.

10.2.4 Expert Reviewers

Expert Reviewer duties include:

1) Reviewing the Method Validation Study Report to determine adequacy and consistency with AOAC RI technical requirements.
2) Reviewing package inserts and user manuals to confirm that the analytical intended use claims in these documents are supported by the Method Developer and Independent Laboratory data and that the package insert requirements are met (Appendix 1).
3) Performing reviews in a timely manner according to the deadlines imposed to the best of their ability.

Expert Reviewers must:

1) Comply with AOAC RI policies and procedures on confidentiality and conflict of interest, including signing a conflict-of-interest policy acknowledgment form.
2) Be willing to devote the time necessary to conduct the data reviews and design testing protocols in a timely manner, as determined by the AOAC RI.
3) Have knowledge of method evaluation processes and have the ability to design and evaluate method evaluation protocols.

4) Have a working knowledge of method evaluation statistics.
5) Have attended the AOAC RI Method Validation Training Course.

Experts selected for a particular method review, in addition to the above, must:

1) Not be employed by or have financial ties with the applicant, competitors, or closely related entities.
2) Not have a regulatory relationship with the applicant firm seeking PTM status.
3) Have technical expertise in the general subject area of the method technology under review.
4) Not routinely use in their work the method that is under evaluation.
5) Understand that multiple review cycles may be required.

Expert Reviewers may be entitled, but not required, to receive a fixed honorarium from the AOAC Research Institute for services performed. One honorarium is offered per method. Experts wishing to serve as reviewers may submit an application through the AOAC RI webpage.

If the originally assigned Expert Reviewers cannot reach agreement on a recommendation to grant or deny PTM status, then the AOAC RI Senior Director will direct the Technical Consultant to assign additional reviewer(s) to provide a deciding recommendation.

10.2.5 AOAC Volunteer Experts

PTM reviews are coordinated with the appropriate AOAC Volunteer Expert from the AOAC OMA program to ensure consistency between programs and between methods.

In addition to the requirements for Expert Reviewers in Section 10.2.4, AOAC Volunteer Expert duties include:

1) Replying to technical questions about the validation outline.
2) Reviewing the Validation Outline.
3) Reviewing the Method Validation Study Report to determine adequacy and consistency with AOAC technical requirements.
4) Reviewing package inserts and user manuals to confirm that the analytical performance claims in these documents are supported by the Method Developer and Independent Laboratory data and that the package insert requirements are met (see Appendix).
5) Determining modification levels and data required, if any, to validate modifications.

10.2.6 AOAC RI Independent Laboratories

Independent Laboratories perform the Independent Validation Study according to the approved protocol(s) from the Validation Outline.

Independent Laboratory duties include:

1) Performance of the Independent Validation Study in accordance with the AOAC Independent Laboratory Agreement.
2) Preparation of the Independent Laboratory Report including the details of the study conducted, the data, and the statistical analyses.
3) Troubleshooting to determine the cause of unexpected results.
4) Timely responses to questions that arise during preparation or review of the Method Validation Study Report.

Independent Laboratories must:

1) Not have a financial or business relationship with the applicant, except as a customer.
2) Not have a regulatory relationship with the applicant firm seeking PTM status.
3) Have technical expertise in the general subject area of the method technology under review.
4) Not routinely use in their work the method that is under evaluation.
5) Have expertise, preferably ISO 17025:2017 accreditation, in the reference method(s) used for comparison studies.
6) Have attended the Method Validation Training Course and be on the list of Approved AOAC RI Independent Laboratories.

10.3 Confidentiality

All documents generated by AOAC RI or received by the AOAC RI from the Method Developer and/or Licensee containing proprietary or confidential information shall be clearly marked as "CONFIDENTIAL".

The AOAC RI considers the following items to be confidential information and therefore subject to this policy:

1) The names of test kit methods and their manufacturers: a) with candidate methods under review; b) who are discussing the possibility of submitting a method for review; or c) who have submitted a method that the AOAC RI has declined to certify.

2) The contents of data submissions; the results of independent testing; the comments of Expert Reviewers and/or Independent Laboratories; and the progress or status of test kit methods under evaluation.

3) The progress of negotiations on license, indemnification, or other agreements with specific test kit manufacturers; including the fact of, and progress of an appeal by a test kit manufacturer.

If there is any doubt as to whether information in any form is confidential, it should be handled as confidential information until the AOAC RI Senior Director determines otherwise.

10.3.1 Access to Confidential Information

AOAC RI employees, volunteers, and Technical Consultants are expressly forbidden to discuss any confidential or proprietary information with AOAC INTERNATIONAL staff employees, Directors, or Board members, or with any other persons who are not directly involved in the evaluation of the method and who have not executed an AOAC RI Nondisclosure Agreement. Employees of AOAC RI Technical Consultants are contractually obligated by the nondisclosure clause of the contract between their employer and the AOAC RI.

10.3.2 Sanctions to Release Information

AOAC RI employees, volunteers, and contractors may release confidential or proprietary information only if: 1) the release is specifically sanctioned by a majority vote of the AOAC INTERNATIONAL Board of Directors, who may decide to disclose confidential information for purposes of resolving AOAC RI business that cannot be resolved otherwise; or 2) with specific permission from the Method Developer.

The Method Developer will be consulted if the AOAC INTERNATIONAL Board is considering the release of confidential information, and the Method Developer will be notified if confidential information is released.

This notice will include a copy of the information that was released, who it was released to, and an explanation of why the information was released.

10.3.3 AOAC Volunteer Experts and Expert Reviewers

Volunteer Experts and Expert Reviewers are required to sign a Nondisclosure Agreement. In addition, the AOAC RI requires that Volunteer Experts and Expert Reviewers adhere to this policy.

Upon completion of the evaluation of a candidate method, Expert Reviewers are required to delete all files and shred any printed materials.

AOAC Volunteer Experts may maintain files on a local secure server for as long as they serve as Volunteer Experts. Any printed confidential materials must be shredded before recycling.

10.3.4 Technical Consultants

All Technical Consultants are required to sign a contract that includes a nondisclosure clause, which is binding on the employees of the Technical Consultant. In addition, the AOAC RI requires that all Technical Consultants adhere to this policy, including the document handling procedures of section 10.3.5.

Upon completion of a contract or project, Technical Consultants are required to upload all confidential files to the AOAC RI secured network. Any printed confidential materials must be shredded before recycling.

10.3.5 In-House Document Handling

Electronic communications and electronic document submissions via email or the AOAC RI website are preferred. The following practices will be followed.

Computer Files:
Confidential document files are stored on secure computer networks. Access is limited to AOAC RI staff and Technical Consultants.

When copying or printing confidential documents, misprints or unwanted copies must be shredded before being recycled.

Mail:
Envelopes and enclosed confidential or proprietary materials should be stamped "Confidential" by the addresser. When receiving confidential materials, the materials are carefully handled to ensure that only the addressee or those working directly with the program have access to the documents.

No confidential material will be circulated in office reading files. All circulated documents should have no references to manufacturers or methods.

Document Storage:

All printed confidential documents, unless shredded and recycled, are stored in locked file cabinets or other secure storage facilities during non-business hours. Access to secure documents is limited to persons who are directly involved in the evaluation of a method and have executed an AOAC RI Nondisclosure Agreement.

10.3.6 Telephone Calls and Video Conferencing

Employees, Technical Consultants, and volunteers of the AOAC RI may not identify methods or test kit manufacturers who are participating in the AOAC RI method validation programs. The AOAC RI does not recommend one certified method over another. If callers request confidential information, or if a person is unsure if requested information is confidential, a message should be taken and the AOAC RI Senior Director consulted.

Revision Date: November 10, 2022

Appendix: Package Insert Requirements

Performance Tested Methods[SM] Program

PACKAGE INSERT REQUIREMENTS

The test kit insert should include the following items, when applicable:

Intended User - Specify the intended user, such as farmer, milk processor, analytical laboratory, etc.

Environmental Factors – Describe any environmental limitations for conduct of the method e.g., temperature, humidity, sunlight, ventilation, separation of work areas, etc.

Applicability - Identify the analyte, mode of measurement (e.g., detection or quantitation) and matrixes (e.g., specific foods or feeds, specific beverages, specific environmental surfaces, wastewater, etc.) for which the kit has been validated.

Limitations - Include precautionary statements on potential interferences and other known limitations of the test.

Instructions - Include complete instructions on how to conduct the test from sample preparation to data interpretation. Describe the use of any internal or external quality control features.

Shelf Life - Include expiration date and storage conditions for the test kit and all associated components.

Limit of Detection and Limit of Quantitation - Express in concentration units (percent, mg/kg, CFU/g, etc.) the limits of detection and quantitation for each matrix. These statements should agree with the supporting data.

Precautions - Provide warnings of safety concerns, disposal instructions, and potentially hazardous steps or components.

Technical Assistance - Provide information (email address, internet address, and/or telephone number) where the user can obtain technical assistance.