FDA Office of Foods and Veterinary Medicine
Method Validation Subcommittee Charter

PURPOSE

The purpose of this charter is to describe the structure and function for the Chemistry Methods Validation Subcommittee (CMVS) and the Microbiology Methods Validation Subcommittee (MMVS).

BACKGROUND

The CMVS and the MMVS are arms of the Foods and Veterinary Medicine (FVM) Chemistry Research Coordinating Group (CRCG) and the Microbiology Research Coordinating Group (MRCG), respectively. Each reports directly to the Foods and Veterinary Medicine Science and Research Steering Committee (SRSC). The list of Advisory Groups for the CRCG and CMVS is outline in Figure 1. The list of Advisory Groups for the MRCG and MMVS is outline in Figure 2.

SCOPE

The primary function of the method validation subcommittees (MVS) is to oversee and coordinate all multi-laboratory validation studies associated with the FDA Foods and Veterinary Medicine Program that fit the criteria described below (*see* PROCEDURES). Such criteria include but may not be limited to multi-Center, cross-cutting applications, and high impact utility in terms of changing the analytical landscape in regulatory testing. The validation process is only applicable to those methods intended for use in a regulatory context. The process will not apply to methods for which regulatory action or decisions are not expected. Additionally, preliminary investigation of the feasibility of new methods would not be covered by this process, but would be expected to be included in an approved CARTS project. Other exceptions may be considered on rare occasions *e.g.* when requested by the SRSC or a technical advisory group (TAG) for the Single-Laboratory Validation (SLV) of a high impact method to support a pressing regulatory gap.

In addition to guidance provided by the CRCG and MRCG, each MVS will also receive input from a wide range of U.S. Food and Drug Administration (FDA or the Agency) stakeholder groups (*i.e.* TAGs) associated with method needs to support outbreak, surveillance, and compliance needs. A representative, but not comprehensive, listing of TAGs that will work closely with each of the MVSs can be found in Appendices I and II.

RESPONSIBILITIES

- Assemble an annual methods validation plan, based on the yearly prioritization process which is aligned with the Food and Veterinary Medicine Strategic Plan, and submit to the SRSC for review and prioritization.
- Evaluate proposals for Multi-Laboratory Validation (MLV) studies of chemical and microbiology methods; this would normally include the evaluation of all associated SLV results among other factors.

- Ensures adherence of the MLV studies to the Foods and Veterinary Medicine Program's "Chemistry Methods Validation Guidance" or "Guidelines for Validation of Analytical Methods for the Detection of Microbial Pathogens in Foods".
- Coordinates chemical and microbiology MLV studies.
- Provides chemical and microbiological method validation guidance and coordination and when necessary, act as a mediator to help resolve disputes over method validation issues.
- Evaluate completed MLV packages for chemical and microbiological methods submitted for approval.

ORGANIZATION/STRUCTURE

- The CMVS reports to the CRCG; the MMVS reports to the MRCG.
- Each MVS will consist of at least 6 voting members including the chairperson, with at least one representative from the Office of Foods and Veterinary Medicine (OFVM), the Center for Food Safety and Applied Nutrition (CFSAN), The Center for Veterinary Medicine (CVM) and the Office of Regulatory Affairs (ORA).
- The CMVS:
    - Will consist of representatives from the major analytical areas in food chemistry: pesticide/contaminant testing, veterinary drug residue testing, persistent organic pollutant/trace testing, and toxic element testing.
    - Will meet on an as-needed basis to discuss and/or assess proposed validation studies, completed validation studies, and submitted questions or concerns regarding method validation issues; however, meetings are intended to be held quarterly at a minimum.

- The MMVS:
    - Will consist of representatives from the major analytical areas in food and veterinary microbiology: microbiology, mycology, and virology; at least one virologist will be on the committee.
    - The MMVS will meet at a minimum on a bimonthly basis to discuss and/or assess proposed validation studies, completed validation studies, and submitted questions or concerns regarding method validation issues.

- One statistician advisor will be made available for consultation as needed.
- Each MVS may utilize the services of an SRSC project manager as needed.
- In special circumstances, either MVS may add an additional voting member on an as-needed basis when a method validation study is submitted in a specialized area (e.g. Color method validation, platform/instrument expert, etc.).
- A quorum of members must be in attendance for official actions. A quorum is achieved when at least half of the members are present. At least one member from ORA must be present or have their vote cast by proxy for a quorum to be recognized.
- A member can vote by proxy when they cannot be present.
- MVS member appointments and chairperson selection will be made by the CRCG and the MRCG in consultation with the SRSC.
- The respective MVS chairperson and voting members shall serve for a term of two years.

- Technical Advisory Groups (TAGs) will be used to leverage their subject matter expertise. Their roles and responsibilities as they pertain to method development and validation are defined in **Appendix IV**. Please note that any input/recommendations/evaluations provided by the TAG will be regarded as important subject matter expert opinions by the MVS when this group makes its final assessment on a method of interest.

PROCEDURES

- All submissions will be made through the subcommittee chairperson. To ensure an efficient and timely review process, all validation-related submissions to the MVS should conform to a standard format as shown in **Appendix III**.
- Information on a submitted validation proposal, completed package or question/concern is distributed to the rest of the group. Submissions are evaluated by all members of the MVS; however, an in-depth review is performed by the member whose specialty coincides most closely with the area of the submission. The Chair (or designated Co-Chair) will assign the in-depth reviewer in each case. The information may consist of a recommendation/assessment forwarded by a TAG along with the original submission.
- If a subject matter expert (SME) is required from outside of the group (*i.e.* to be the in-depth reviewer) the Chair will work with the MVS to identify a suitable candidate to serve in a temporary capacity.
- A reasonable timeframe for a review of a proposal/finished package should be two to four weeks. Timely turnaround of reviews is important.
- If any member of the MVS has any questions regarding the submission during the evaluation phase, they can ask the chairperson or project manager to take the question directly to the submitting party (either the Chair of the TAG if one was involved or the direct submitter of the validation package). The original question and the acquired answer will be shared with all members of the MVS.
- Any other reports submitted by the collaborating TAG such as progress reports on performance of a newly validated method in a program area or recommendations on needed method development to fill gaps are logged and filed by the MVS chairperson or project manager and shared during regular MVS meetings.
- At the conclusion of the evaluation phase, the MVS Chair and project manager arrange for a meeting to discuss the new submission and the group makes a decision on how to proceed.
- At the MVS evaluation meeting, the in-depth reviewer presents their assessment first followed by a general group discussion. Please note that any input, recommendations, or evaluations provided by a TAG will be used as important SME opinions by the MVS when this group makes its final assessment.
- MVS meetings may also be called when a TAG initiates dialogue and solicits concurrence on method validation proposals. MVS makes a decision on whether the proposed method validation is truly needed and will enhance an existing program area and/or fill an analytical gap. The decision is again captured in a memo and transmitted back to the TAG soliciting input.

VALIDATION EVALUATION CRITERIA

Evaluation of method validation proposals
The criteria considered by either MVS in evaluating submissions of *proposed method validation studies* will include the following:

- *Impact to Agency mission*: Does the method improve regulatory testing in some area such as efficiency, cost, scope, technical merit, *etc*? Additionally, does the proposed methods validation align with OFVM, CVM, CFSAN and/or ORA science priorities?
- *Quality of the results from the laboratory validation study:* Are the method's performance parameters acceptable as outlined in the Foods and Veterinary Medicine Program's "Chemistry Methods Validation Guidance" or "Guidelines for Validation of Analytical Methods for the Detection of Microbial Pathogens in Foods".
- *Analytical strategy*: Consider effectiveness of chosen platform, ease of implementation, sensitivity and accuracy, evaluate selectivity and specificity, availability of selected reagents from reliable commercial sources, environmental considerations, *etc.*
- *Harmonization /consolidation of methods:* Is a new stand-alone method needed or can the proposed method be consolidated into an existing method by performing a matrix extension?
- *Novel scope:* Is the method going to create a new area of testing? Is it going to expand the matrix/analyte scope of existing methods?

The study will be entered into CARTS upon approval of a method validation protocol by the MVS and will be formally tracked for progress.

The proposal will receive another round of review in CARTS through the established approval chain used by each Center (See Figure 1). Once the CARTS reviews are performed and permission granted by all channels, the project will be officially in CARTS and will be formally tracked for progress.

If a favorable review on a proposed MLV study is not granted at any point in this pathway (at the local management stage, at the TAG stage, at the MMVS stage or at the CARTS review stage, the project will be retracted. Submitters will have the option of modifying/editing the proposal/research goals based on feedback and re-submitting.

Decisions of the MVS are captured in memo form and transmitted through the submitting party's line management chain with a copy to the TAG Chair, if one is involved, and the appropriate RCG Chair.

Evaluation of completed method validation packages
The criteria considered by the MVS in evaluating completed method validation packages will include the following:

- Has the validation study demonstrated that the method is "fit for intended use"? Does the method clearly show that the chemical(s)/organism(s) in the scope can be recovered and detected in all relevant matrices in the scope at the sensitivity required to meet regulatory and/or health/hazard thresholds?

- Does the validation study follow the Foods and Veterinary Medicine Program's " Program's "Chemistry Methods Validation Guidance" or "Guidelines for Validation of Analytical Methods for the Detection of Microbial Pathogens in Foods", as appropriate? Does the validated method have properly identified acceptance criteria for the validation elements that were met?
- Scientific recommendations of the TAG (or other SMEs), if involved in the review.
- Does the validation package follow the original proposal that was submitted and approved? Use the criteria above for proposed studies if this is not available.
- Quality of results obtained from the MLV study.

The desired contributions of the TAGs to the mission of MVS are outlined in **Appendix IV** and also contain similar criteria for evaluating proposals and completed validation packages (See Figure 2).

RECORDS

- The MVS Chair will assure that the activities of the MVS and TAGs, including submissions, recommendations, decisions, issues, action items and other pertinent materials, are documented and communicated to senior management and relevant staff as appropriate.
- All finished validated methods that are incorporated into compliance testing will be made available to the public via posting on FDA's website.
- All internal communications/documents/decisions/memos generated during the evaluation of a validation proposal and/or finished validation package will also be compiled on a secure internal FDA website for future reference.

END NOTE

- The MVS will review this Charter at least bi-annually based on experience gained and revise it as necessary.

Figure 1. Flowchart of *Validation Study Proposal* Submission Process Involving a Technical Advisory Group as an Intermediary

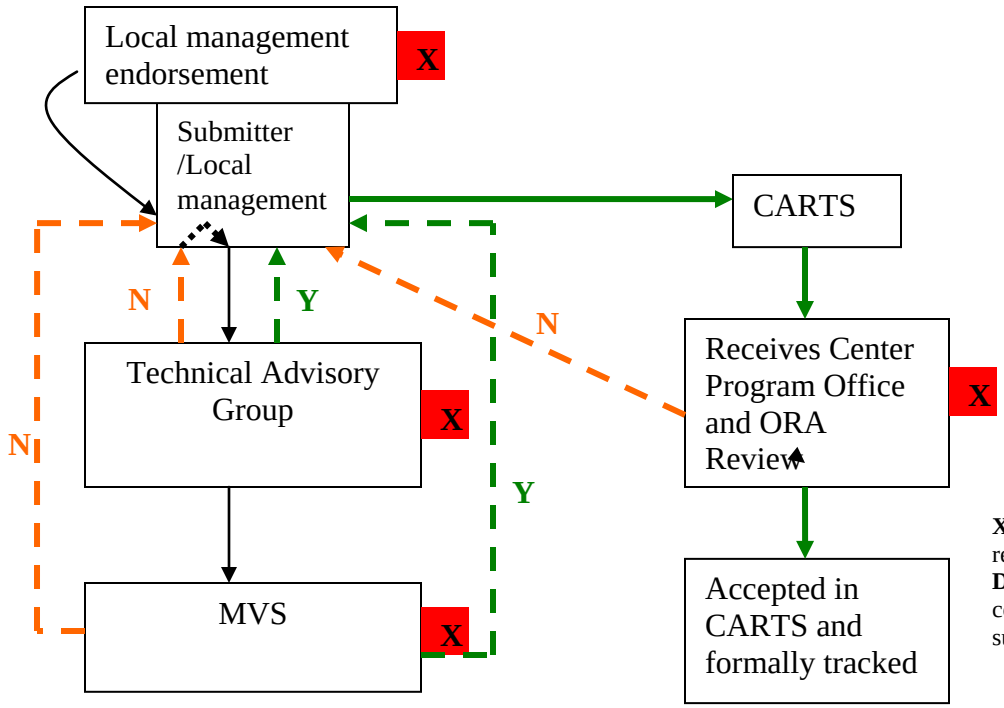
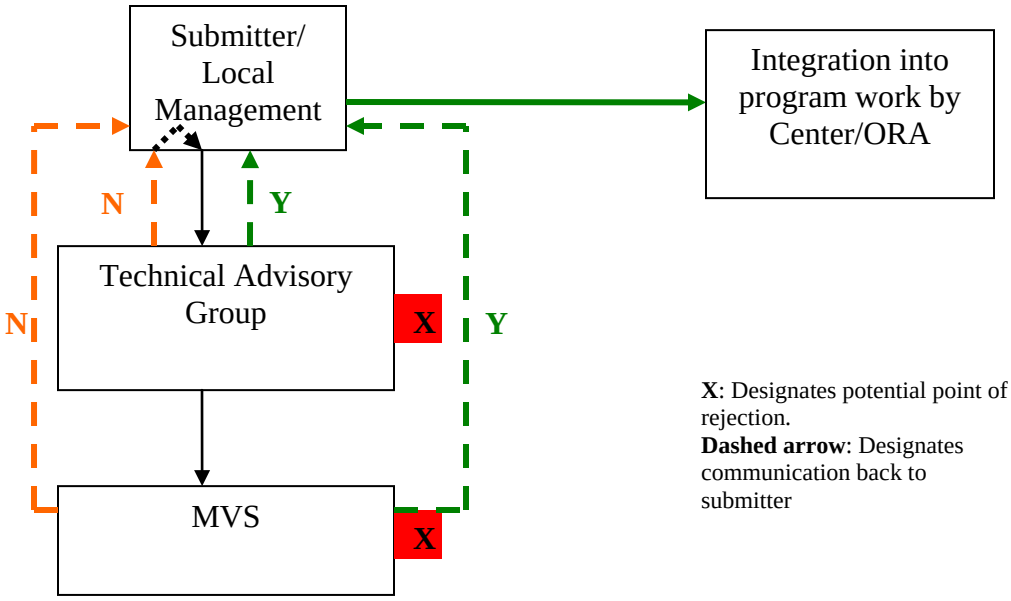


Figure 2. Flowchart of *Completed Validation Package* Submission Process Involving a Technical Advisory Group as an Intermediary



APPENDIX I

Current Advisory Groups including TAGs for the Chemistry Research Coordinating Group (CRCG) and the Chemistry Method Validation Subcommittee (CMVS)

NOTE: All committees listed below are current (as of March, 2014). Periodic updates including the addition of newly formed TAGs, when needed, will be posted on the OFVM's web pages separate from this document. Amendments to this list can be found on OFVM Science and Research SharePoint Site; http://sharepoint.fda.gov/orgs/OFVM-Science/SitePages/Home.aspx

1. **Allergens and Gluten Methods TAG**
2. **Aquaculture Research TAG**
3. **ORA Chemandos**
4. **DNA-based Species Identification TAG**
5. **Persistent Organic Pollutants TAG**
6. **Economic Adulteration TAG**
7. **Elemental Analysis Steering Committee TAG**
8. **Field Food/Feed Committee**
9. **Food Emergency Response Network (FERN)**
    a. **Chemistry Cooperative Agreement Program (cCAP)**
    b. **Food Emergency Response Network (FERN) Method Coordination Committee (MCC)**
10. **Interagency Residue Control Group (IRCG)**
11. **Mycotoxins Methods TAG**
12. **ORA Method Development and Validation Program (MDVP)**
13. **Pesticides Steering Committee TAG**
14. **Portable Devices TAG**
15. **Seafood Methods TAG**
16. **Veterinary Drugs and Feed TAG**
17. **Veterinary Laboratory Response Network (Vet-LRN)**

APPENDIX II

Current Advisory Groups including TAGs for the Microbiology Research Coordinating Group (MRCG) and the Microbiology Method Validation Subcommittee (MMVS)

NOTE: All committees listed below are current (as of March, 2014). Periodic updates including the addition of newly formed TAGs, when needed, will be posted on the OFVM's web pages separate from this document Amendments to this list can be found on OFVM Science and Research SharePoint Site; http://sharepoint.fda.gov/orgs/OFVM-Science/SitePages/Home.aspx)

1. **Bacteriological Analytical Manual Council (BAM Council)**
2. **C-bot TAG**
3. **Drug Resistance TAG**
4. **Field Food/Feed Committees**
5. **Food Emergency Response Network (FERN) Microbiology Cooperative Agreement Program (mCAP)**
6. **Food Emergency Response Network (FERN) Method Coordination Committee (MCC)**
7. **High-impact Pathogens TAG**
8. **Listeria TAG**
9. **Molecular Epidemiology TAG**
10. **Next Generation PCR TAG**
11. **OMICS TAG**
12. **ORA Method Development and Validation Program**
13. **ORA Micronauts**
14. **Next Generation PCR TAG**
15. **Salmonella TAG**
16. **STEC TAG**
17. **Veterinary Laboratory Response Network (Vet-LIRN)**
18. **Virology TAG**
19. **Processing Controls TAG**

<u>APPENDIX III</u> – **Standard Template for Validation Proposal/Finished Package Submission** *(Example only. A fillable pdf can be found on the OFVM Science and Research SharePoint Site; http://sharepoint.fda.gov/orgs/OFVM-Science/SitePages/Home.aspx)*

Food & Veterinary Medicine
Science and Research Program

Application for FVM Method Validation Proposal/Finished Package Review

Method Title:	Submission Date *(dd/mmm/yyyy)*:
Title of project linked to method:	
CARTS No:	
Author(s) / Point(s)-of-Contact:	

CONTACT INFORMATION

Center:	
Address:	
Phone No:	
Email Address:	

SUPERVISORY CONCURRENCE

Immediate Supervisor:	
Title:	
Phone No:	
Email Address:	
Signature	

SRSC RCG CONCURRENCE

RCG Chairperson:	
Phone No:	
Email Address:	
Signature	

METHOD DESCRIPTION

Part 1

Discipline	Chemistry - Microbiology - Nanotechnology - Toxicology *(circle one)*
Applicable Validation Level (refer to appropriate validation guidelines)	
Target Analyte	
Food Matrix/Matrices	
Technology used (e.g. HPLC, ELISA, PCR, etc.)	

Part 2

Please describe in detail all aspects of the method to be validated to include but not limited to sensitivity, selectivity, special equipment needs, custom reagents, and safety needs. Attach all preliminary and/or single laboratory validation data to this application. A justification to support initiating a validation study must be included in this section. Refer to the section "Validation Evaluation Criteria" of the FVM Method Validation Subcommittee Charter.

APPENDIX IV – Leveraging Existing Technical Advisory Groups (TAGs)

PRE-STAGE (this is the "solicitation" stage):

1) Identify method validation gaps in program areas – communicate to SRSC/MVS
2) Upon concurrence from SRSC/MVS, solicit method validation efforts in the specific identified areas from Center and ORA researchers
3) Triage the incoming method validation proposals and prioritize them based on the following criteria:
    a. Does the submitted proposal have local (*i.e.,* local laboratory management) endorsement?
    b. Does the submitted proposal address a method gap?
    c. Are there other similar methods in use? If so, can the proposed method be consolidated into existing methods? If the proposed method is a stand-along new method, how does it differ from existing methods? What improvements, if any, does the new proposal bring? The desired mode of operation in regulatory testing is minimum number of methods each with a large scope in terms of matrix and analyte as such broad-band methods promise to extract the most information out of a single collection and possibly put the agency in a pro-active stance when it comes to uncovering threats to consumer health.
    d. Is the submitted protocol in compliance with the Agency-wide Method Validation Guidance document?
    e. Is the scope of the proposed method (both the analyte and product/matrix scope) sufficient for the program area it is intended for?
    f. Is the instrument platform selected appropriate for the intended purpose?
    g. Does the submitting laboratory have the necessary expertise to execute the proposal?
    h. Does the submitting laboratory have the necessary collaborations in place and have these collaborators been evaluated as appropriate partners?
    i. Will the submitting laboratory be able to allocate the necessary resources to finish the validation within proposed timelines?
    j. Does the submitter have a proposal that would enable effective distribution of the method to other FDA laboratories and for integration into the program area it is intended for?

POST-STAGE (this is the “evaluation” stage):

1) Assign a focus group of up to three individuals to review the submitted validation package. The focus groups should be composed of individuals that were not involved in the validation work in order to preserve objectivity.
2) Identify a deadline by which the focus group should finish the review and submit a report of their assessment to the TAG. A reasonable timeframe for a review of a proposal should be two weeks and for a review of a finished validation package should be four weeks. Timely turnaround of reviews is important to ensure uninterrupted progress of research.
3) Conduct a discussion of the highlights of the assessment of the focus group with all members of the TAG. Identify any changes/edits the focus group may need to make in the assessment based on comments from the TAG.
4) Submit the TAG-supported assessment of the focus group to MVS/SRSC.
5) MVS/SRSC will directly notify the submitter/local management chain of its decision with a carbon copy to the involved TAG. If the validation package is accepted by the MVS/SRSC, track the effectiveness of its performance and its scope of use in the relevant program area and report back to MVS.

Approval

This Charter is approved by the Chief Science Officer/Research Director, OFVM. The MVS Chair is responsible for maintaining the Charter, updating the Charter as needed, and disseminating updated Charters to Primary Members and other Stakeholders as required.

APPROVED BY:

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David White, Chief Science Officer/Research Director, OFVM *Date*