Sections included in this document (Change History)

1. Summary

This document establishes and describes the standard operating procedure (SOP) for the approval and tracking of the Foods Program analytical method development proposals for implementation in U.S. Food and Drug Administration (FDA or the Agency) laboratories for regulatory compliance, enforcement and surveillance purposes. An important component of this process will include coordinated alignment of the method(s) to be developed with Center and Program needs and with identified Agency priorities.

2. Scope/Policy

This SOP applies to all method development activities across the FDA Foods Program regulatory science enterprise comprised of the laboratory operating units of the Center for Food Safety and Applied Nutrition (CFSAN) in conjunction with the food and feed operations of the Center for Veterinary Medicine (CVM) and the Office of Regulatory Affairs (ORA). The Foods Program Regulatory Science Steering Committee (RSSC), formerly known as the Foods Veterinary Medicine (FVM) Science and Research Steering Committee (SRSC), will provide direct oversight to all cross-center project collaborations and all methods validation processes deemed necessary through the appropriate Research Coordination Group (RCG).

Preliminary, short-term or exploratory investigations that focus on the feasibility of a new method and/or technology and any subsequent single laboratory validation (SLV) study may be managed wholly by the respective Center and Office line management structure; these activities follow approved Center/Office policies, which may include documentation within online databases such as the Component Automated Research Tracking System (CARTS).

All relevant presentations and publications associated with method development research will be electronically attached to CARTS or CVM research management system.

The FDA Foods Program (CFSAN, CVM, or ORA) line management will ensure that there is appropriate communication and collaboration between the applicable technical advisory groups (TAGs) (*e.g.* Bacteriological Analytical Manual (BAM) Council, Pesticide Technical Advisory Group, etc.) and that the investigator reviews CARTS for similar research projects before any studies are proposed and entered in CARTS. This type of communication is especially critical in emergency response activities.

The FDA Foods Program enterprise recognizes it must demonstrate (through defined validation studies) that all methods used to support regulatory actions meet agency requirements and are fit for their intended use. However, this SOP is a forward-looking document; the requirements described here will only apply to newly developed methods and not existing methods. Whereas most FDA Foods Program analytical methods currently employed for regulatory applications have not been validated by the new standards described herein and in the Foods Program Methods Validation Guidelines, their documented performance over the course of many years of use provides the necessary evidence to support their reliability. Previously developed and validated methods met the quality standards defined and required at the time they were developed and adopted for use and have been demonstrated through time and application for their intended use. However, this document defines criteria for methods development and validation as of this document's effective date. Moving forward, the continued assessment of current methods, future method needs (i.e. modifications, extensions, and incorporation of advanced technologies) will require the RCGs, associated TAGs, and the respective Methods Validation Subcommittee (MVS) to make recommendations on validation criteria to be fulfilled and what past methods may be subjected to reevaluation. However, it is also recognized that in some instances, the circumstances may dictate use of emergency-use validated or single-lab validated methods for regulatory purpose. The goal is to move all methods used routinely in regulatory testing to a MLV status, however, the timeframe to do so may sometimes proceed use in regulatory testing.

An important way to bring together use of old methods and those covered in this forward-looking document is through the FDA Foods Program Compendium of Analytical Laboratory Methods (https://www.fda.gov/food/laboratory-methods-food/foods-program-

compendium-analytical-laboratory-methods) and the Foods Program Laboratory Methods pages (https://www.fda.gov/food/science-research-food/laboratory-methods-food). All methods that are validated under the Foods Program MDVIP should be documented in the Foods Program Compendium. There will be small differences between the approaches used in the Chemistry and Microbiology Programs. However, all methods validated under the MDVIP should be incorporated into these outward facing web resources. It is recommended that older methods that have been used extensively in FDA regulatory laboratories be evaluated by RCGs/TAGs for their validation equivalence to current Foods Program Methods Validation guidelines and as much as possible be incorporated into the Foods Program methods pages.

This SOP is intended to provide guidance and instructions to FDA staff and represents current Agency thinking on this topic. It does not create or confer any rights for any person and does not operate to bind the FDA or the public in any way. An alternative approach may be used if such an approach satisfies the requirements of applicable statutes and regulations. It is intended for use by FDA personnel, but may be made available electronically to the public.

3. Responsibilities

Foods Program Governance Board

- Provides real and visionary strategic direction to the RSSC and constituent components of the FDA Foods Program (CFSAN, CVM, and ORA)
- Acts as an oversight body

Foods Program Regulatory Science Steering Committee, RSSC

- Responsible for providing strategic direction and leading the coordination of methods development activities across the Foods Program and ensuring integration of Center research and methods development with corresponding ORA activities
- Ensures overarching coordination of methods development and validation efforts across the Foods Program
- Acts as the final decisional body in cases that cannot be resolved at the RCG level
- Reviews overall method development and validation work on an ad hoc basis to ensure alignment of activities with the Foods Program and Agency goals
- Provides summary reporting on method development and validation activities to the Foods Program Governance Board as needed

Research Coordination Groups, RCGs (Microbiology, Chemistry)

- Responsible for coordinating the Foods Program method development activities to ensure that new methods are identified and used in compliance programs and assignments
- Oversee the process of approving methods for posting to the Foods Program Compendium of Analytical Laboratory Methods
- Ensure recommendations from the RCG and TAGs are communicated to respective Centers and office line management

RCG Methods Validation Subcommittees, MVS (Microbiology, Chemistry)

- Has an oversight responsibility for MLV studies. Refer to Foods Program RSSC document titled, "FDA Foods Program Methods Validation Subcommittee Charter"
- Charged with developing and updating Foods Program Methods Validation Guidelines based on recommendations made by the appropriate RCG

Respective Center and Office Line Management

- Ensures an appropriate collaboration between the Center(s) and ORA
- Ensures the investigator reviews Foods Program' s research management systems (e.g. CARTS) for similar research projects and consults with the appropriate TAG, if applicable, before initiation of any method development activities
- Ensures project entry, progress reporting, and tracking activities are completed in a timely manner

Technical Advisory Groups, TAGs

- Act collaboratively without Center or Office bias as a technical advisory body to the RCGs, MVSs, and the RSSC
- Collectively represent the subject matter experts (SME), state-of-the-art knowledge base, including knowledge of any best practice(s), for a technical area within the FDA

Principal Investigator (PI)

- Performs methods development research and method validation studies to improve analytical capabilities of the program including, as appropriate, service to stakeholders
- Must be cognizant of all quality assurance (QA) and quality control (QC) criteria that must be met for any method to be considered suitable for regulatory use

FDA Method Validation Core Style Entity (MVCSE)

- Serves as an independent laboratory responsible for planning and execution of activities for the validation of chemical and microbiological analytical methods developed by Foods Program researchers and intended for regulatory compliance when requested for more complex methods
- Assists the RSSC through the Chemistry or Microbiology MVS in the methods validation activities, and works collaboratively with the RCG, TAGs and PI.

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4. Procedures

The process for identifying and prioritizing the annual listing of method development/validation needs for the review and approval of the Annual Methods Development and Validation Plan (AMDVP) and for the overall method development through validation and implementation are described below and illustrated in Attachments 1 and 2. Briefly, Attachment 1 illustrates the coordinated oversight roles of the Foods Program Governance Board, RSSC, RCGs, and MVSs in the method development process. Attachment 2 provides more detailed depictions of the entire Foods Program regulatory science enterprise, the process defined for the individual Center level, SLV study level, the MLV study level, and the ORA implementation phase.

4.1 General Policy and Program Guidance

Identification and Prioritization of Method Development and Validation Needs

The RSSC will oversee the assembly and prioritization of an annual list of method development and validation needs derived from activities associated with the Annual Technical Meeting of the Foods Program RSSC and on an ad hoc basis. This will include all aspects of the Foods Program regulatory science enterprise. This listing will be periodically updated and disseminated to all Foods Program-related research centers as it is recognized that these activities will require substantial cross-center collaboration for successful development, validation, and implementation. Proposals to address these needs can be submitted at any time through Center-specific review processes and then into the appropriate research management system for consideration and tracking.

- The RCGs or appropriate subcommittees will assemble an AMDVP based on the yearly research coordination process.

- Method development/validation work in response to emergent situations (e.g., foodborne disease outbreak, natural disasters, etc.) may take priority over other activities.

Exploratory Investigations

Individual Center/Office personnel may explore new technologies or develop new methods (up to and including an SLV study) under their independent discretionary investigations and research process, however:

- It is line management's responsibility to ensure that the proposed project has programmatic value.
- Line management will ensure appropriate collaboration between the Center(s) and ORA in identifying a recognized method gap and defining the proposed method's "fit-for-purpose" criteria, including relevant quality standards.
- Line management will ensure that the investigator performs a thorough search of active and archived projects in the appropriate research management system to prevent duplicative efforts and to identify potential opportunities for collaboration.
- It is recommended that line management and the investigator consult with all appropriate RCG(s) and/or TAG(s) prior to the initiation of any new methods project.
- All research projects will be submitted and approved through the research management system.
- Outcomes of exploratory investigations must be reported in the research management system.

Cross-Center Collaborations or MLV Initiatives

- Methods that are deemed suitable for regulatory application and that have been successfully evaluated at the single laboratory validation level will be considered for an MLV study in accordance with current Foods Program validation protocols.
- All MLV activities intended to address specific needs identified by the RSSC must be jointly developed by appropriate collaborators.
- All MLV studies will be coordinated with and overseen by the respective MVS.
- Line management and the investigator, in coordination with the appropriate RCG and/or MVS chair, should establish a timely process for review, comment and concurrence of submitted MLV proposals and the associated action plans.

- Under certain circumstances with proper allocation of resources, line management and the investigator have an option to arrange with the MVCSE to undertake and complete the MLV studies, in coordination with the appropriate RCG and/or MVS chair.
- Prior to initiation of an MLV, mechanisms for funding MLVs must be thoroughly discussed at the RCG level, and if necessary, at the RSSC level to ensure that all stakeholders understand the funding approach and there is consensus to support that approach.
- Prior to initiation of an MLV, the relevant RCG should work with Center RSSC members to communicate workplanning requirements for the MLV to the relevant Center Compliance Office, who will work their ORA counterparts. This will ensure that MLV plans are prioritized appropriately in the overall ORA laboratory workplan.
- All approved MLV activities must be entered into CARTS and tracked.
- The RSSC will be the final decisional body in cases that cannot be resolved at the MVS or RCG level; disputes will be handled as per the conflict resolution clause in the RSSC Charter.

Reporting & Oversight

- The Chairs of the Chemistry and Microbiology RCGs will make presentations to the RSSC on a semi-annual basis, at a minimum. These presentations will include MVS reviews and evaluations of overall method development and validation progress to ensure alignment with the Foods Program strategic goals and priorities.
- Progress reports will be submitted through CARTS on a semi-annual basis.
- Respective Center/Office scientific leadership will review and evaluate method development and validation progress and outcomes on an annual basis. Actions may include redirection or termination of studies that are not making sufficient progress or have been identified as no longer consistent with current strategic priorities or needs of the Foods Program.
- The RSSC will report updates on method development and validation to the Foods Program Governance Board on an annual basis.

4.2 Identifying and Prioritizing Method Development and Method Validation Needs

Center components of the Foods Program Directorate and ORA are responsible for identifying and documenting a prioritized listing of strategic method development and validation needs for their respective programs annually. It will be left to the discretion of each individual component as to the process by

which annual methods development and validation priorities are established. The RSSC will announce yearly submission deadlines and will not be less than 30 days prior to the Annual Technical Meeting of the Foods Program RSSC. Method development and validation needs that are provided by Center components of the Foods Program Directorate and ORA will be consolidated, reviewed, and discussed by scientific and programmatic leaders invited to the Annual Technical Meeting with the goal of providing an overall strategic plan for the upcoming fiscal year. Investigators, with line management approval, are encouraged to develop and submit cross-cutting proposals in support of the methods development needs identified during the Annual Technical Meeting of the RSSC. Emergent or unplanned program needs can be identified and communicated to the RSSC at any time throughout the year.

4.3 Development, Review, and Approval of the Annual Methods Development and Validation Plans

RCGs will develop a prioritized list of method development needs following the Annual Technical Meeting of the RSSC. The RCGs will work with the MVSs to ensure that the methods development needs are aligned with Foods Program and Agency strategic goals and objectives. This activity will be part of the yearly plan formally presented to the RSSC for review and approval. Following approval, the RSSC communicates the plans to the Foods Program regulatory science enterprise. As needed, these plans may be updated by the RCGs with review and approval by the RSSC.

4.4 Implementation of Multi-laboratory Validated Methods

Successful completion of collaborative multi-laboratory validated methods provides a basis for discussion of implementation of the method in compliance programs and in ORA laboratories for regulatory applications. In most, but not all, cases, initiation of an MLV indicates a need for implementation. Using the Foods Program Method Implementation Guidelines, discussion between the various MDVIP components shall develop an implementation plan, if there is agreement that the method will serve a necessary programmatic purpose.

Once an implementation plan is developed, ORA shall facilitate appropriate Quality Management System (QMS) and line management approvals, coordinate Compliance Program Guidance revisions as necessary, and then implement and benchmark new methods in regulatory applications. ORA shall communicate method implementation results to Foods Program stakeholders – internal and external, as appropriate. ORA will manage the integration of newly approved methods into the field laboratories, and be responsible for developing and implementing quality assurance and training plans; implementation may include, but not be limited to, the following items:

1. Plan for purchasing instruments (if necessary)
2. Training plans
3. Assure QA & QC criteria are addressed and satisfied
4. Proficiency testing plan
5. Assessment and reporting of method performance/program impacts

4.5 Foods Program Method Compendium and Foods Program Laboratory Methods Pages

The Foods Program RSSC will maintain a Foods Program Compendium of Analytical Laboratory Methods on the outward facing www.FDA.gov site. This page will be a subset of a Foods Program Laboratory Methods site that will include the Compendium, Validation Guidelines and other related methods information that is important to FDA and its external stakeholders. The RSSC will designate a lead member to work with the CFSAN web team to maintain this site. Each RCG will have a member or team who will be responsible for policies related to methods posting to these sites and will work through the RSSC lead to update these sites. All methods posted to these sites will include information about validation status and the duration for which the method will be posted. It is recommended that only methods having undergone MLV should be indefinitely posted; other methods should have a limited duration posting (1-3 years) to ensure that efforts are made to elevate these methods up to MLV status. For historical reasons, the Bacteriological Analytical Manual (BAM) will be part of the Compendium and will remain the final destination for microbiological methods. However, the microbiology portion of the Compendium will have a section for microbiological methods that have undergone MLV but are not yet ready to be incorporated into the BAM. In general, all methods undergoing a successful MLV will be posted to the Compendium. Each RCG will establish policy for methods that have SLV, emergency-use or lesser validation status, and establish the appropriate location on these sites for posting. Every effort should be made to be as transparent as possible about the methods the FDA Foods Program uses in its laboratories.

5. Records

Annual Methods Development and Validation Plans

CARTS entries (proposals, status, and final reports, etc.) related to individual methods development and validation activities

Original Data & Method Validation Files and Approvals
Reports of Implementation of New Methods

6. Supporting documents

FDA Foods Program Method Validation Guidelines for Microbial Pathogens

FDA Foods Program Guidelines for the Validation of Chemical Methods

Guidelines for the Validation of Analytical Methods for Nucleic Acid Sequence-Based Analysis of Food, Feed, Cosmetics and Veterinary Products

Method Implementation Guidelines for Foods Program Methods Development, Validation, and Implementation Program (MDVIP)

FDA Foods Program Regulatory Science Steering Committee (RSSC) Charter

FDA Foods Program Microbiology Research Coordination Group Charter

FDA Foods Program Chemistry Research Coordination Group Charter

FDA Foods Program Method Validation Subcommittees Charter

Membership of Foods Program Research Coordination Groups and Technical Advisory Groups

ORA Laboratory Manual

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7. Attachments

Attachment 1.
Oversight of FDA Foods Program Method Development, Validation, and Implementation Activities

Attachment 2.
Summary Diagram of MDVIP Processes

Document History					
Version #	**Status (I, R, C)**	**Date Approved**	**Location of Change History**	**Name & Title**	
				Author	**Approving Official**
1.0	I	10/16/2014	N/A	SRSC MDV Process Development Subcommittee	SRSC
2.0	R	03/16/2021	Substantial Changes in Responsibilities and Procedures Sections	RSSC MDVIP SOP Revision Subcommittee	RSSC

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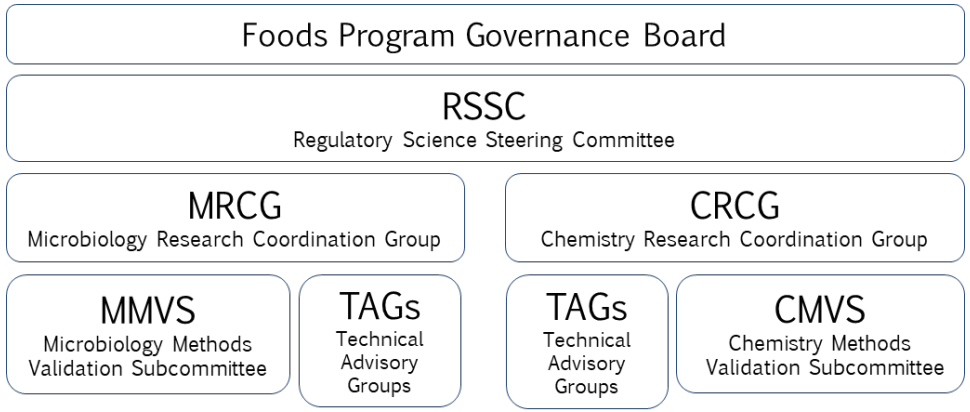
Document Owner:
Foods Program Regulatory Science Steering Committee

Contributing Authors:
Foods Program Regulatory Science Steering Committee and subsidiaries

Attachment Figure Graphic File:
MDVIP Process Map Updated033121

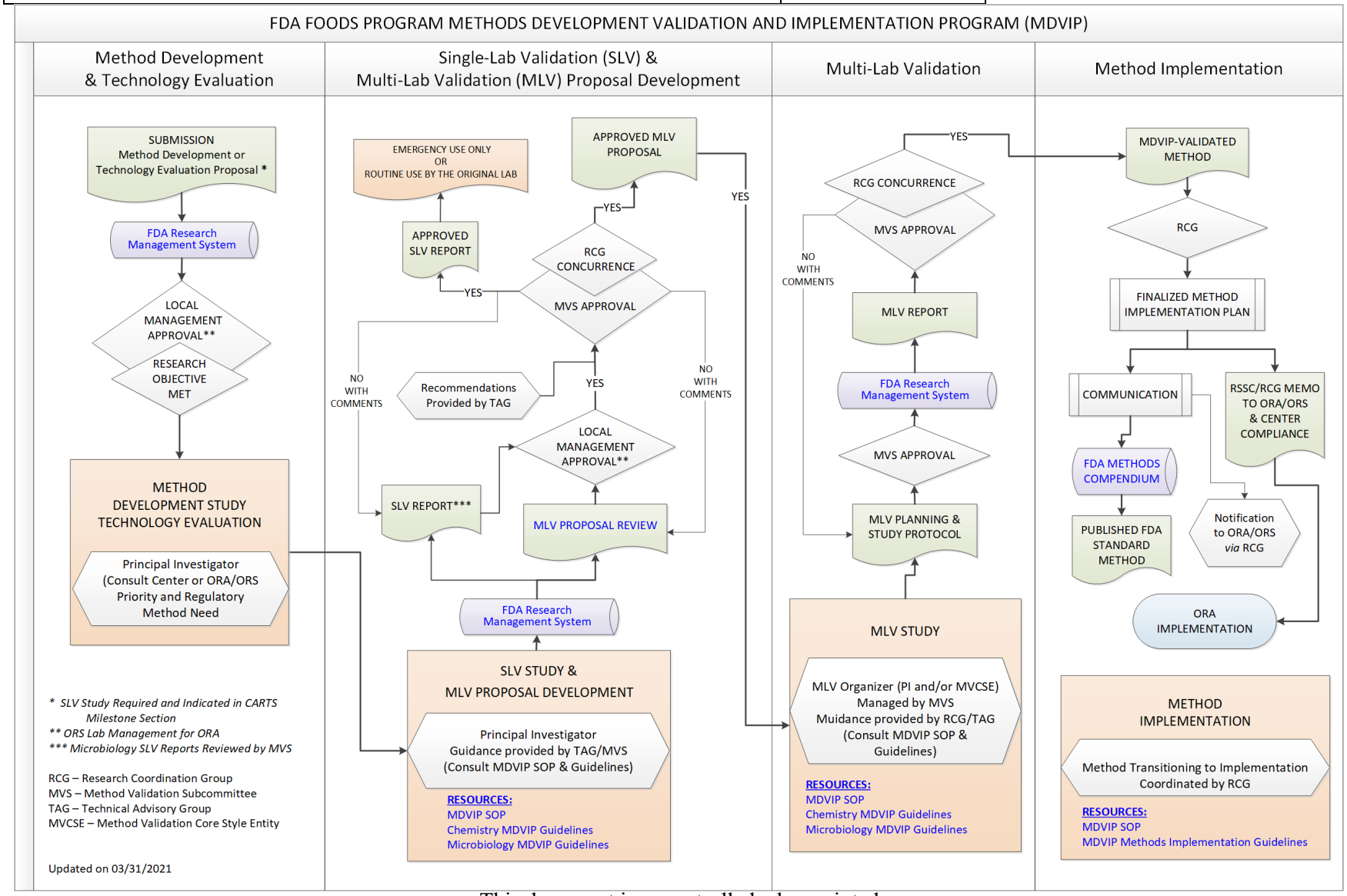
Attachment Figure Graphic File Owner:
Sunee Himathongkham

This diagram illustrates the oversight bodies of Foods Program method development, validation, and implementation activities. It depicts the integrated and coordinated relationship between the Foods Program Governance Board, the Regulatory Science Steering Committee (RSSC), the Research Coordination Groups (RCGs), Methods Validation Subcommittees (MVSs) and appropriate Technical Advisory Groups (TAGs). Identification of method gaps and the establishing alignments for their development is a major focus for the RSSC and relies on considerable input, evaluation, and approval from the operational organizations (CFSAN, CVM, ORA) with additional appropriate representation from the National Center for Toxicological Research under the Office of the Chief Scientist.



Part 1: Methods Development Process. Part 2: Single-Laboratory Validation and MLV Proposal Development Process; Part 3: Multi-Laboratory Validation Process; Part 4: Methods Implementation Process.

This diagram highlights MDVIP processes for method development, performance evaluation of methods at the Single-Laboratory Validation (SLV), Multi-Laboratory Validation (MLV) proposal development, MLV, and the implementation of a new method in ORA/ORS laboratories. The identification of methods gaps includes but are not limited to, the principal investigator, line management (Center, Office, Division) and Technical Advisory Group (TAG). Such method development activities will remain a Center-specific concern through the Single-Laboratory Validation (SLV) stage. The decision for any newly developed method to proceed to an MLV is the sole responsibility of the Regulatory Science Steering Committee (RSSC) made in consultation with the appropriate Research Coordination Group (RCG), Method Validation Subcommittee (MVS) and the TAG. Decision disagreements will be resolved as described in the RSSC Charter. All MLVs will be managed by the appropriate MVS. The implementation phase of a newly developed, successfully validated method will be coordinated by the RCG and guided by the principles and practices established by ORA as published within the ORA laboratory manual. This diagram also illustrates the overarching role of the FDA Foods Program Research Management Systems such as the Component Automated Research Tracking System (CARTS), throughout the process.


FDA FOODS PROGRAM METHODS DEVELOPMENT VALIDATION AND IMPLEMENTATION PROGRAM (MDVIP)
Method Development & Technology Evaluation
Single-Lab Validation (SLV) & Multi-Lab Validation (MLV) Proposal Development
Multi-Lab Validation
Method Implementation
SUBMISSION Method Development or Technology Evaluation Proposal *
FDA Research Management System
LOCAL MANAGEMENT APPROVAL**
RESEARCH OBJECTIVE MET
METHOD DEVELOPMENT STUDY TECHNOLOGY EVALUATION
Principal Investigator (Consult Center or ORA/ORS Priority and Regulatory Method Need
* SLV Study Required and Indicated in CARTS Milestone Section
** ORS Lab Management for ORA
*** Microbiology SLV Reports Reviewed by MVS
RCG – Research Coordination Group
MVS – Method Validation Subcommittee
TAG – Technical Advisory Group
MVCSE – Method Validation Core Style Entity
Updated on 03/31/2021
EMERGENCY USE ONLY OR ROUTINE USE BY THE ORIGINAL LAB
APPROVED MLV PROPOSAL
APPROVED SLV REPORT
RCG CONCURRENCE
MVS APPROVAL
YES
NO WITH COMMENTS
Recommendations Provided by TAG
LOCAL MANAGEMENT APPROVAL**
SLV REPORT***
MLV PROPOSAL REVIEW
FDA Research Management System
SLV STUDY & MLV PROPOSAL DEVELOPMENT
Principal Investigator Guidance provided by TAG/MVS (Consult MDVIP SOP & Guidelines)
RESOURCES:
MDVIP SOP
Chemistry MDVIP Guidelines
Microbiology MDVIP Guidelines
RCG CONCURRENCE
MVS APPROVAL
MLV REPORT
FDA Research Management System
MVS APPROVAL
MLV PLANNING & STUDY PROTOCOL
MLV STUDY
MLV Organizer (PI and/or MVCSE) Managed by MVS Muidance provided by RCG/TAG (Consult MDVIP SOP & Guidelines)
RESOURCES:
MDVIP SOP
Chemistry MDVIP Guidelines
Microbiology MDVIP Guidelines
MDVIP-VALIDATED METHOD
RCG
FINALIZED METHOD IMPLEMENTATION PLAN
COMMUNICATION
RSSC/RCG MEMO TO ORA/ORS & CENTER COMPLIANCE
FDA METHODS COMPENDIUM
PUBLISHED FDA STANDARD METHOD
Notification to ORA/ORS via RCG
ORA IMPLEMENTATION
METHOD IMPLEMENTATION
Method Transitioning to Implementation Coordinated by RCG
RESOURCES:
MDVIP SOP
MDVIP Methods Implementation Guidelines