	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 1 of 14
Title: Methods Development, Validation, and Implementation Program		Effective Date: 10/16/2014 Revised: 09/30/2014	

Sections included in this document/(Change History)

1. Summary
 2. Scope/Policy
 3. Responsibilities
 4. Procedures
 5. Records
 6. Supporting documents
 7. Attachments
- Document history

1.
Summary


This document establishes and describes the standard operating procedure (SOP) for the approval and tracking of Foods and Veterinary Medicine (FVM) 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 FVM laboratory science enterprise comprised of the operating units of the FVM Directorate [the Office of Foods and Veterinary Medicine (OFVM), the Center for Food Safety and Applied Nutrition (CFSAN), and the Center for Veterinary Medicine (CVM)], in conjunction with the foods and veterinary medicine operations of the Office of Regulatory Affairs, ORA. The FVM Science and Research Steering Committee (SRSC) will provide direct oversight to all Cross-Center Project Collaborations and all Multi-Laboratory Validation (MLV) 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; however, any and all such activities are expected to be processed within the Component Automated Research Tracking System (CARTS).

All relevant presentations and publications associated with method development research will be electronically attached to the appropriate CARTS entry.

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 2 of 14
Title: Methods Development, Validation, and Implementation Program		Effective Date: 10/16/2014 Revised: 09/30/2014	

FVM 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 Steering Committee, etc.) and that the investigator reviews CARTS for similar research projects *before* any studies are proposed and entered into CARTS. This type of communication is especially critical in emergency response activities.


The FDA FVM 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 of FDA FVM analytical methods currently employed for regulatory applications have not been validated by the new standards described herein and in the methods validation guidelines (see links to methods validations guidelines in Section 6), 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 the effective date. Moving forward, the continued assessment of current methods, future method needs (i.e. modifications, extensions, and the 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.

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 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

FVM Program Executive Council, FPEC:

- Provides real and visionary strategic direction to the SRSC, and constituent components of the FDA Foods and Veterinary Medicine Program (CFSAN, CVM, and ORA)
- Provides approval of the Annual Methods Development Plan (AMDP)
- Acts as an oversight body
- Involves the FVM Governance Board in decision-making, as appropriate

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 3 of 14
Title:		Effective Date: 10/16/2014 Revised: 09/30/2014	
Methods Development, Validation, and Implementation Program			

OFVM Science and Research Team

- Resides within OFVM
- Responsible for providing strategic direction and leading methods development activities across CFSAN, CVM and ensuring integration of Center research and methods development with corresponding ORA activities
- Responsible for assembling and tracking progress of the AMDP

FVM Program Science and Research Steering Committee, SRSC:

- Acts as the final decisional body in cases that cannot be resolved at the RCG level
- Reviews overall method development and validation work twice a year to ensure alignment of activities with FVM Program and Agency goals
- Provides summary reporting on method development and validation activities to the FPEC on an annual basis
- Ensures overarching coordination of methods development and validation efforts across the FVM Program

Research Coordination Group, RCG (e.g. Microbiology, Chemistry, etc.):

- Ensures AMDP is aligned with the FVM Strategic Plan and provides clearance for submission to the SRSC
- Ensures recommendations from the RCG and TAGs are communicated to respective Centers and office line management

RCG Methods Validation Subcommittees, MVS:


- Has an oversight responsibility for MLV studies. Refer to FVM document titled, "[FDA Office of Foods and Veterinary Medicine Method Validation Subcommittees Charter](#)"
- Charged with prioritizing method validation needs based on recommendations made by the appropriate RCG

Respective Center and Office Line Management:

- Ensures that there is appropriate collaboration between the Center(s) and ORA
- Ensures that the investigator reviews CARTS for similar research projects and consults with the appropriate TAG, if applicable, before initiation of any method development activities
- Ensures CARTS project entry, progress reporting, and tracking activities are completed in a timely manner

Technical Advisory Groups, TAGs:

- Acts collaboratively without Center or Office bias as a technical advisory body to the RCGs, MVSs, and the SRSC
- Collectively represents 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

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 4 of 14
Title:		Effective Date:	
Methods Development, Validation, and Implementation Program		10/16/2014 Revised: 09/30/2014	

Investigator(s):

- Perform 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

4. Procedures

The process for identifying and prioritizing the annual listing of method development/validation needs; and, for the review and approval of the AMDP are described below and illustrated in Attachments 1 through 5. Briefly, Attachment 1 illustrates the coordinated oversight roles of the FPEC, SRSC, RCGs, and MVSs in the method development process. Attachments 2 through 5, provide more detailed depictions of the entire method development enterprise (Attachment 2); the process defined for the individual Center level (Attachment 3); the MLV study level (Attachment 4), and ORA implementation phase (Attachment 5).

4.1 General Policy and Program Guidance


Identification and Prioritization of Method Development and Validation Needs

The SRSC will oversee the assembly and prioritization of an annual list of method development and validation needs derived from activities associated with the Annual FVM Program Research Prioritization Conference; and, on an ad hoc basis. This will include all aspects of the FVM science and research enterprise. This listing will be periodically updated and disseminated to all FVM 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 CARTS for consideration and tracking.

- The RCGs, or appropriate subcommittees, will assemble an AMDP, based on the yearly prioritization process
- Method development/validation work in response to emergent situations (e.g., melamine, 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:

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 5 of 14
Title:		Effective Date:	
Methods Development, Validation, and Implementation Program		10/16/2014 Revised: 09/30/2014	


- 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 methods 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 CARTS 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
- It is recommended that line management and the investigator, in coordination with the appropriate RCG and/or TAG chair, establish a timely process for review, comment and concurrence of submitted project proposals
- All research projects will be submitted and approved through CARTS
- Outcomes of exploratory investigations must be reported in CARTS

Cross Center Collaborations or MLV Initiatives

- All regulatory MLV activities intended to address specific needs identified by the SRSC must be jointly developed by appropriate collaborators
- Methods that are deemed suitable for regulatory application and that have been successfully evaluated at the single laboratory validation level will be considered for a MLV study in accordance with current FVM Program validation protocols
- 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
- All approved MLV activities **MUST** be entered, into CARTS and tracked
- The SRSC 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 SRSC Charter

Implementation of Validated Methods

- Methods that have successfully completed the MLV stage are acceptable for official analyses
- Upon successful completion and approval of an MLV, the method will be communicated in the appropriate on-line guidance manual and compliance program guidance

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 6 of 14
Title:		Effective Date:	
Methods Development, Validation, and Implementation Program		10/16/2014 Revised: 09/30/2014	

- 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

Reporting & Oversight


- The Chairs of the Chemistry, Microbiology, Toxicology and Nanotechnology RCGs will make presentations to the SRSC 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 FVM strategic program goals and priorities
- Progress reports will be submitted through CARTS on a semi-annual basis
- Respective Center 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 FVM Program
- SRSC will report updates on method development and validation to the FPEC on an annual basis.

4.2 Identifying and Prioritizing Method Development and Method Validation Needs

Center components of the FVM 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 SRSC will announce yearly submission deadlines and will not be less than 60 days prior to the Annual FVM Program Research Prioritization Conference.

Method development and validation needs that are provided by Center components of the FVM Directorate and ORA will be consolidated, reviewed, and discussed by scientific and programmatic leaders invited to the Annual FVM Research Prioritization Conference with the goal of providing an overall strategic plan for the upcoming fiscal year.

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 7 of 14
Title: Methods Development, Validation, and Implementation Program		Effective Date: 10/16/2014 Revised: 09/30/2014	

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 FVM Research Prioritization Conference.

Emergent or unplanned program needs can be identified and communicated to the SRSC at any time throughout the year.

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

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

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

MVSs for each RCG will develop a prioritized list of method validation needs in consultation with the appropriate RCG following the Annual FVM Program Research Prioritization Conference. The RCGs will work with the SRSC to ensure that the validation needs are aligned with FVM and Agency strategic goals and objectives. This activity will be part of the yearly plan formally presented to the FPEC for review and approval. Following FPEC approval, the SRSC communicates the plans to the FVM regulatory science enterprise. As needed, these plans may be updated by the MVS with review and approval by the respective RCG and the SRSC.


4.5 Implementation of Multi-laboratory Validated Methods

Successful completion of collaborative multi-laboratory validated methods shall provide a full and sufficient basis for implementation of the method in compliance programs and in ORA laboratories for regulatory applications. 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 FVM Program stakeholders – internal and external, as appropriate.

5. Records

Annual Methods Development Plans

Annual Methods Validation Plans

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 8 of 14
Title:		Effective Date: 10/16/2014 Revised: 09/30/2014	

Methods Development, Validation, and Implementation Program

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

[Office of Foods and Veterinary Medicine Method Validation Guidelines for Microbial Pathogens](#)

[Office of Foods and Veterinary Medicine Guidelines for the Validation of Chemical Methods](#)

[Office of Foods and Veterinary Medicine Microbiology Research Coordination Group Charter](#)

[Office of Foods and Veterinary Medicine Chemistry Research Coordination Group Charter](#)

[Office of Foods and Veterinary Medicine Method Validation Subcommittees Charter](#)

[Membership of Foods and Veterinary Medicine Research Coordination Groups and Technical Advisory Groups](#)

[Foods and Veterinary Medicine \(FVM\) Science and Research Steering Committee \(SRSC\) Charter](#)


[ORA Laboratory Manual](#)

7. Attachments

Attachment 1. Summary Diagram – Part 1: Development and Approval of the Annual Methods Development Plan and Oversight of Foods and Veterinary Medicine Program Method Development Activities through the Science and Research Steering Committee, Research Coordination Groups and the Foods and Veterinary Program Medicine Executive Council

Attachment 2. Summary Diagram – Part 2: Method Development Processes. Separate Processes for New Method, Technology Exploration, or Single Laboratory Validation Activities and for Joint Collaborations or Regulatory/Multi-Laboratory Validation Efforts with Implementation in Regulatory Laboratories

Attachment 3. Proposal, Review, Approval, and Reporting of Methods Development and Validation Activities: Single-Center activities

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE Page 9 of 14
Title: Methods Development, Validation, and Implementation Program		Effective Date: 10/16/2014 Revised: 09/30/2014	

Attachment 4. Proposal, Review, Approval, Reporting, and Implementation of Methods Development and Validation Activities: Multi-Laboratory Validation and Collaborative activities

Attachment 5. Office of Regulatory Affairs Implementation of a New Method

Document history					
Version #	Status (I, R, C)	Date Approved	Location of Change History	Name & Title	
				Author	Approving Official
0	I		N/A	SRSC MDV Process Development Subcommittee	SRSC

Electronic Version/Filename:

Methods Development-Validation-Implementation Program_v09-30-2014.doc

Last edited by:

Nelson, Chad P.

Last edit date/time:

09/30/2014 11:25 PM

Document Owner:

David.White@fda.hhs.gov

Contributing Authors:


William.Martin@fda.hhs.gov;Palmer.Orlandi@fda.hhs.gov;Gregory.Diachenko@fda.hhs.gov;Steven.Musser@fda.hhs.gov;
David.White@fda.hhs.gov;Chad.Nelson@fda.hhs.gov;Philip.Kijak@fda.hhs.gov;Donald.Zink@fda.hhs.gov;
Douglas.Heitkemper@fda.hhs.gov

Attachment Figure Graphic File:

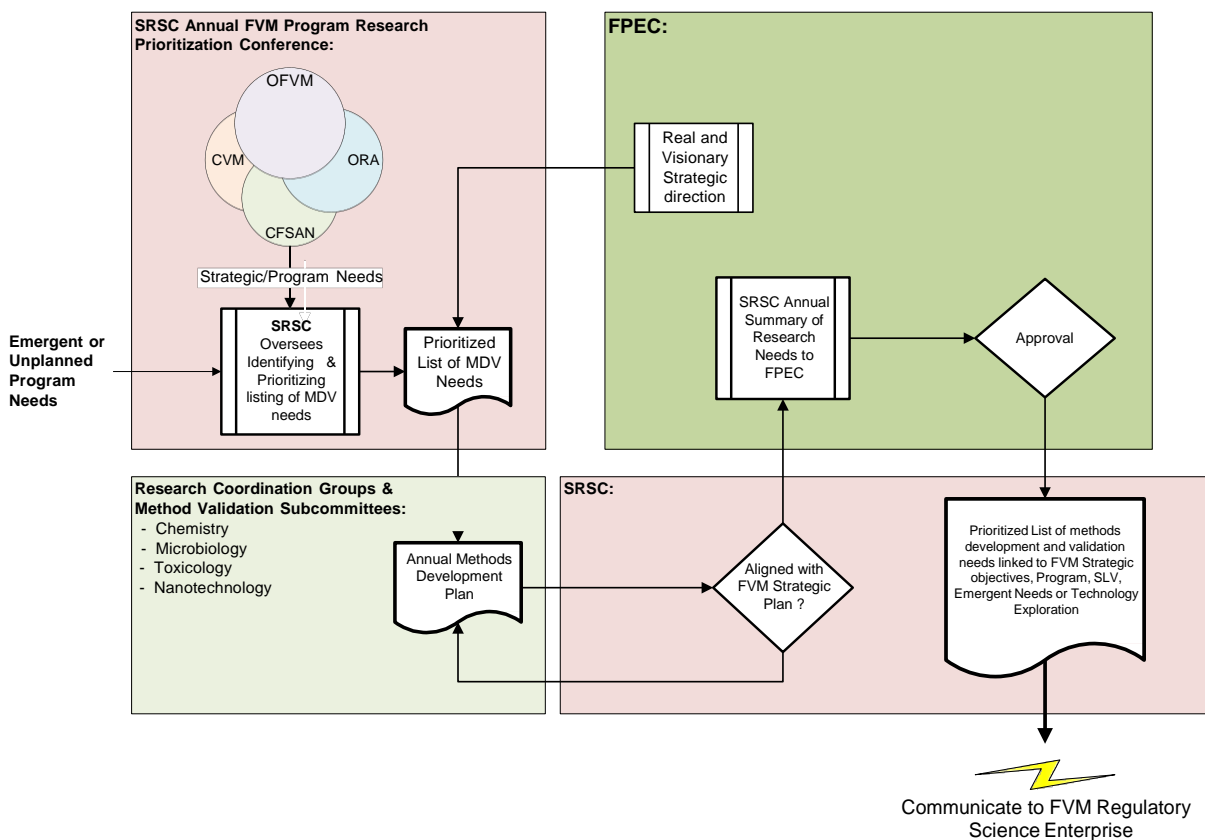
FDA-OFVM-3_MDV Program_v0 Attachments_02-21-2014.vsd (Microsoft Visio file)

Attachment Figure Graphic File Owner:


Nelson, Chad P.

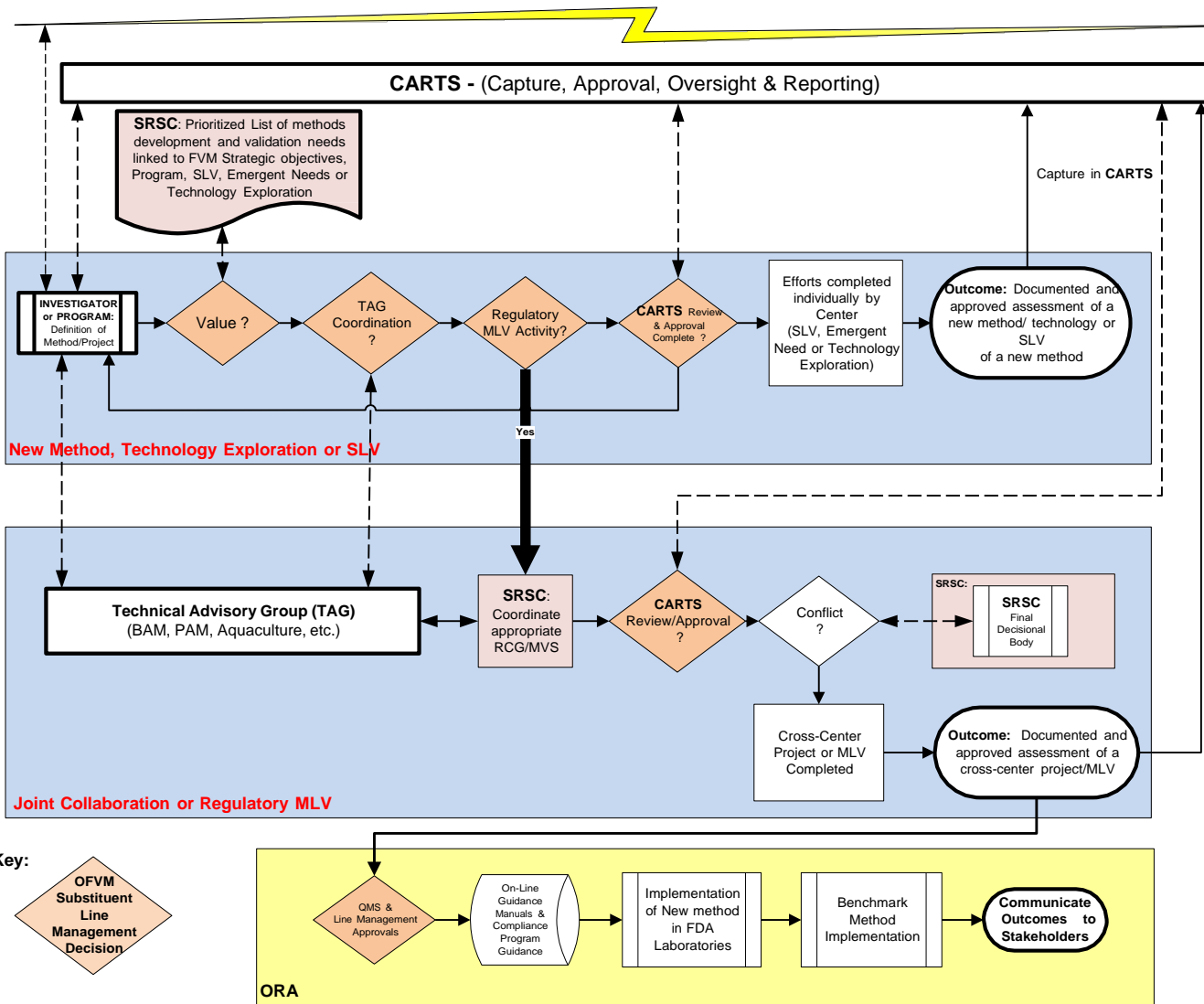
 <p style="text-align: center;">PROGRAM-WIDE PROCEDURE (Contains Non-binding Recommendations) Office of Foods and Veterinary Medicine</p>	Document #:	Version #: 0
	FDA-OFVM-3	INITIAL RELEASE Page 10 of 14
Title: <p style="text-align: center;">Attachment 1. Summary Diagram – Part 1: Development and Approval of the Annual Methods Development Plan and Oversight of Foods and Veterinary Medicine Program Method Development Activities through the Science and Research Steering Committee, Research Coordination Groups and the Foods and Veterinary Medicine Program Executive Council</p>		Effective Date: 10/16/2014 Revised: 09/30/2014

Identification and Prioritization of MDV Needs:




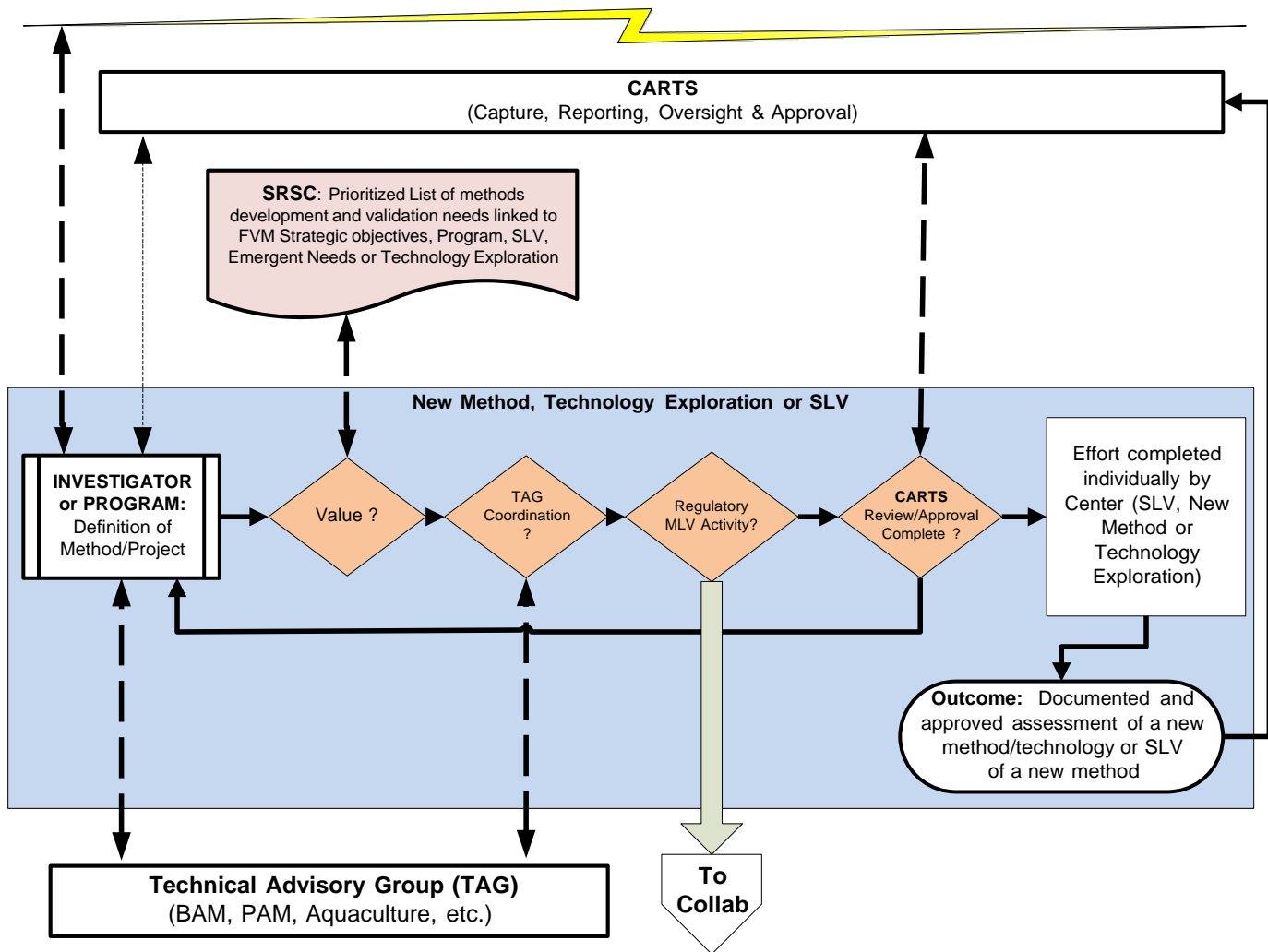
This summary diagram illustrates the development and approval process of the Annual Methods Development Plan. The diagram also depicts the integrated and coordinated relationship between the FVM Program Executive Council (FPEC), the Science and Research Steering Committee (SRSC), the Research Coordination Groups (RCGs) and their Validation Subcommittees. Identification of method gaps and the establishing priorities for their development is a major focus for the SRSC during the annual FVM Program Research Prioritization Conference and relies on considerable input, evaluation, and approval from the operational organizations (CFSAN, CVM, ORA), the RCGs, and the FPEC, respectively, with additional appropriate representation from the National Center for Toxicological Research, the Office of International Programs, and the Office of the Chief Scientist.

 PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #: FDA-OFVM-3	Version #: 0 INITIAL RELEASE Page 11 of 14
	Title: Attachment 2. Summary Diagram – Part 2: Method Development Processes. Separate Processes for New Method, Technology Exploration, or Single Laboratory Validation Activities and for Joint Collaborations or Regulatory/Multi-Laboratory Validation Efforts with Implementation in Regulatory Laboratories	




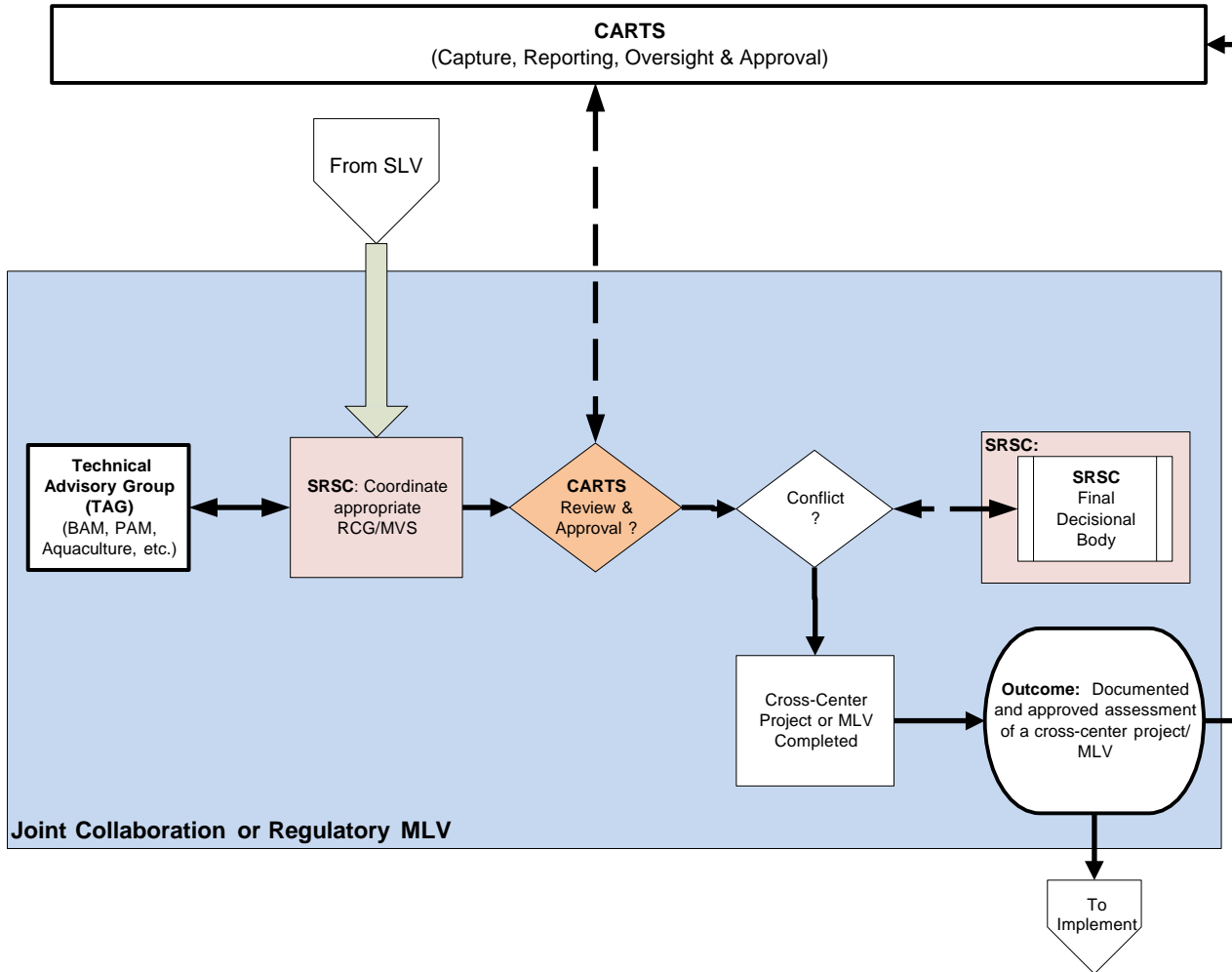
This summary diagram highlights the sequential steps for evaluating the need for a new method, associated planning and research activities, method validation, and the implementation process. This diagram also illustrates the overarching role of the Component Automated Research Tracking System (CARTS) throughout the process.

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE
Title: Attachment 3. Proposal, Review, Approval, and Reporting of Methods Development and Validation Activities: Single-Center Activities		Effective Date: 10/16/2014 Revised: 09/30/2014	




This diagram shows the development of a new method, technology and/or project, through to implementation, at the single laboratory validation level. The identification of methods gaps include many consultative aspects that include, but are not limited to, the investigator, line management (Center, Office, Division) and technical advisory group(s). Such method development activities will remain a Center-specific concern through the Single-Laboratory Validation (SLV) stage.

	PROGRAM-WIDE PROCEDURE Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE
Title: Attachment 4. Proposal, Review, Approval, Reporting, and Implementation of Methods Development and Validation Activities: Multi-Laboratory Validation and Collaborative Activities		Effective Date: 10/16/2014 Revised: 09/30/2014	



This diagram illustrates those procedures and processes for performance evaluation of methods at the Multi-Laboratory Validation (MLV) level. The decision for any newly-developed method to proceed to a MLV is the sole responsibility of the Science and Research Steering Committee (SRSC) and will be made in consultation with the appropriate Research Coordination Group (RCG) and Method Validation Subcommittee (MVS), as well as any appropriate TAGs. Disputes will be handled as per the conflict resolution clause in the SRSC Charter. All MLVs will be managed by the appropriate MVS.

	PROGRAM-WIDE PROCEDURE FDA Office of Foods and Veterinary Medicine	Document #:	Version #: 0
		FDA-OFVM-3	INITIAL RELEASE
Title: Attachment 5. Office of Regulatory Affairs Implementation of a New Method		Effective Date: 10/16/2014 Revised: 09/30/2014	

From MLV

ORA:



The implementation phase of a newly developed, successfully validated method will be guided by the principles and practices established by ORA as published within the ORA laboratory manual. This includes adherence to Quality Management System (QMS) such as proficiency testing programs to ensure uniform analytical performance across ORA field laboratories. Methods will become officially adopted by FVM compliance programs and available in the appropriate analytical compendia (e.g. Bacteriological Analytical Manual).

Approval

This document is approved by the FDA Foods and Veterinary Medicine (FVM) Science and Research Steering Committee (SRSC). The FVM SRSC Project Manager is responsible for updating the document as change requirements are met, and disseminating updates to the SRSC and other stakeholders, as required.

APPROVED BY:

<u>//David White// 10/02/2014</u> OFVM Chief Science Officer/Research Director	<u>//William T. Flynn// 10/21/2014</u> CVM, Deputy Director for Science Policy
<u>//Palmer A. Orlandi// 10/02/2014</u> OFVM Senior Science Advisor	<u>//John Graham// 10/09/2014</u> CVM, Director Office of Research
<u>//Donald L. Zink// 10/20/2014</u> CFSAN Senior Science Advisor	<u>//Brian L. Baker// 09/20/2014</u> ORA, Director Office of Regulatory Science
<u>//Vincent K. Bunning// 09/30/2014</u> CFSAN, Director Office of Regulatory Science	<u>//Timothy McGrath// 10/07/2014</u> ORA, Director Food and Feed Scientific Staff
<u>//Kevin Gaido// 10/08/2014</u> CFSAN, Director Office of Applied Research & Safety Assessment	<u>//William B. Martin// 09/30/2014</u> ORA, Member of the ORA Scientific Advisory Council