ORA LABORATORY MANUAL

FDA Office of Regulatory Affairs
Division of Field Science

DOCUMENT NO.: III-06
VERSION NO.: 23
FINAL
EFFECTIVE DATE:
4-2-04
Revised: 12-03-08

Section 6 — ORA METHOD DEVELOPMENT and VALIDATION PROGRAM — Section 6

Contents

6.1 Introduction

As the regulatory agency designated to maintain the safety of the nation's foods, drugs, biologics, medical devices, and radiological products, FDA has broad responsibilities to protect the public health. It is the vision of the Division of Field Science (DFS) to provide a convincing and prevailing scientific, research and analytical base for regulatory decisions that protect and promote public health. Vital to carrying out this vision is the continual development, validation and improvement of methods that support our regulatory responsibilities. The ORA Method Development and Validation Program is designed to satisfy the need for regulatory analytical methods meeting current and anticipated public health program needs and agency priorities. The exploration of new technologies and methods for rapid analyses, as well as hypothesis driven basic studies, are also important components of this science program.

6.2 Purpose

The goal of this program is to satisfy the need for regulatory analytical methods meeting current and anticipated public health program needs and agency priorities. This Laboratory Manual section provides the procedures for the identification, development, submission, review and publication of method protocols, validation studies, method extensions or other research studies. The procedures assure that projects meet regulatory needs, accomplish their intended purpose, include validation for Agency-wide distribution (where appropriate), and become meaningful analytical tools for use. Additionally it provides scientific conduct guidelines for the program and encourages and enhances the creative skills of talented scientists in ORA Laboratories.

6.3 Background and Program Overview

The past method development and validation process was revised in fiscal year 2005 to its current status. The historical research process is described in Field Management Directive 143.

6.3.1 Program Goals

The goals of the Method Development and Validation Program are the following:

- provide opportunities for ORA scientists to develop analytical methodologies and expertise that support the regulatory and public health protection mission of FDA and solve continuing, new, or emerging regulatory problems;
- support FDA Center research through method validation and collaboration with FDA Center scientists;
- upgrade present methods to use improved instrumentation or technology and validate methods to "Standard" method status for FDA use;
- incorporate the developed methods into daily operations; and to transfer the technology, where appropriate, to our stakeholders and customers; and
- develop the knowledge, skills, and abilities of ORA staff analysts.

6.3.2 ORA Method Development and Validation Program and Sources

The sources for MDVP listed below follow the procedures described in sections 6.5 and 6.6.

6.3.2.1 ORA Planned Method Development and Validation Studies

Planned development of methods and studies are designed to handle regulatory program-oriented analytical testing problems. The method or analytical need can be conceived by the ORA analysts, headquarters units, Food Emergency Response Network (FERN), district offices, and Science Advisors. Laboratory Directors determine how their assigned Full Time Equivalents (FTEs) will be used. These resources are allocated in the annual ORA work plan. The outcome of this work may directly affect Center regulatory program development.

6.3.2.2 Compliance Program Directed Method Development and Validation

Method development and validation operations mandated in compliance programs are planned in the Centers and conducted by ORA. The ORA analyst assigned to the project has latitude to plan activities to

explore and solve the problem, but the Center and ORA through DFS, define the parameters for the scope of the study.

Laboratory Directors coordinate collaborations and method development/validation by communicating with the appropriate Center and DFS regarding criteria for validation.

6.3.3 Other Programs Available to ORA for Method Development and Validation

6.3.3.1 District Discretionary Method Development and Validation

In each ORA laboratory's annual work plan, a specified number of hours are assigned per operational scientist to plan and complete method development and validation needs that arise during the year and are not covered by other programs. The Laboratory Manual policies and procedures applicable to method development and validation are followed as well as applicable technology requirements and local procedures. This work is controlled by local management.

6.3.3.2 Field Research Center Method Development and Validation

In the early 1980s, field research centers were established in several ORA laboratories to focus research efforts in support of a variety of program areas. Three field research centers remain: Seafood Products Research Center (Seattle), Animal Drugs Research Center (Denver), and Total Diet and Pesticide Research Center (Kansas City). In addition, the Atlanta Center for Nutrient Analysis performs similar functions in part. The field research centers provide complex analytical support to field laboratories and the Centers, conducting research on current methodology, developing and refining new rapid chemical and biological methodology, conducting and participating in collaborative studies and validation trials of analytical methods, and providing expert technical scientific assistance and consultative services. Each Center's method development programs are independent of the field laboratory process described in this chapter. Projects are defined through meetings with the associated Centers and DFS, or by a call for projects and needs to all field laboratories.

6.3.3.3 Science Advisor Research Associate Program

The Science Advisor Research Associate Program (SARAP) was initiated in 1973 in order to provide field professionals with an opportunity for uninterrupted training and research involvement. The program allows researchers to become or remain current in advancing scientific and technical skills.

The purpose of the SARAP program is the following:

- permit and encourage scientifically competent field employees to develop themselves for research and specialty positions through a planned staff development program;

- upgrade the quality and status of field scientific research development and investigations;
- develop a cadre of well-trained field scientists and investigators capable of meeting the challenges posed by the demand for more complex method development and investigations; and
- introduce new scientific techniques and capability into our field laboratories.

SARAP research can be conducted at a local college or university, FDA laboratory, or a combination of both under the direction of laboratory management, and Science Advisor or other academic professor.

Up to one full FTE of research time may be granted to the SARAP associate. The Associate Commissioner for Regulatory Affairs approves all the necessary funding for SARAP research. (Please refer to SARAP guidelines at DFS).

6.3.3.4 Cooperative Research and Development Agreement

The Federal Technology Transfer Act of 1986, (FTTA), authorizes government agencies to enter into collaborations with the private sector, academic institutions, and other organizations. The mechanism used is known as the Cooperative Research and Development Agreement (CRADA).

A CRADA is used to formalize a specific collaborative project which may involve research leading to new inventions or further development of existing government or non-government inventions in fulfillment of FDA missions. The primary purpose is to transfer the technology and intellectual property to the commercial marketplace. The terms of a CRADA, which are negotiated by FDA and the collaborator, may address patent rights and licensing matters as well as the collaborative research project.

A CRADA is not intended to be a general funding mechanism. CRADA-derived funds are to be used for costs associated with the project specified in the CRADA. Laboratories must be prepared to address the impact to ongoing research if a CRADA and related financial support is terminated unexpectedly. Time allotted to a CRADA project can be taken from a laboratory's discretionary time, planned research allotment, or by agreement with a Center to use other compliance program planned time.

More information can be obtained from http://eric.fda.gov under Acquisition and Grants and under Technology Transfer.

6.4 Roles and Responsibilities

6.4.1 Associate Commissioner for Regulatory Affairs (ACRA) and the Office of Regional Operations (ORO)

The ACRA and the Director of ORO share responsibility for promoting and supporting a strong ORA method development and validation program as well as determining ORA goals.

6.4.2 Regional Food and Drug Directors (RFDDs)

The Regional Food and Drug Directors assign a specific number of FTEs to each laboratory based on past method development/validation accomplishments, laboratory expertise, and agency need in specialty and program areas.

6.4.3 Division of Field Science (DFS)

The Division of Field Science (DFS) develops and implements the method development and validation guidelines and manages the overall program. DFS issues the call for proposals, assigns reviewers and approves proposals, assigns Research Project Numbers (RPN) and compiles and maintains the approved and completed project list.

DFS works with the Laboratory Directors, the Centers, and analysts to guide and assist with the method development and validation process. The Director of DFS is the recommending and approving official for field laboratory method development and validation programs. DFS monitors the various steps in the process, issues requests for proposals, coordinates proposal review, approves projects, and receives progress reports.

6.4.4 ORA Laboratory and Science Branch Directors

Direction and management of the ORA method development and validation resources reside at the local laboratory management level. Laboratory management is responsible for developing and executing their laboratory's method development and validation program. This includes: developing and selecting the most significant projects, providing funding, and assuring that work plan resources are fully planned and executed. Timely planning, direction, and accomplishment of these projects are crucial. Laboratory Directors rely on supervisors, senior laboratory staff, and Science Advisors.

Laboratory management must establish an environment where there is vigorous growth, development, and accomplishment of projects within the laboratories. Recognition that is commensurate with the level of contribution to the regulatory mission of ORA and FDA by scientists who successfully complete method development and validation projects is an important aspect of a successful program.

6.4.5 ORA Analysts

ORA analysts are responsible for the following:

- submitting method development and validation needs in response to DFS' call;
- developing and submitting proposals in accordance with the approved procedures;
- timely accomplishment of approved projects;
- adhering to the highest standards of intellectual honesty and ethical standards in formulating, conducting, and presenting method development and validation work**;** and
- following research and publication requirements and guidelines written in sections 6.5 and 6.6.

6.4.6 Science Advisors

Science Advisors aid laboratory management and analysts by providing technical analytical guidance and method development and validation process guidance at the local level. More specifically, the advisors provide direction towards the development of concept and method development and validation project papers, and assist in the conduct, evaluation, and presentation of method development and validation end-products. They promote interaction and collaborations with their respective universities and other science advisors where appropriate.

Additionally the science advisors recommend improvements towards the method development and validation program, provide periodic follow-up reports regarding method development and validation's regulatory impact including associated publications, presentations, collaborative studies, adoption as official methods by additional field and headquarters laboratories, and inclusion in compliance programs.

6.4.7 FDA Center Scientists

FDA Center scientists respond to DFS' requests for method development and method validation projects involving ORA participation. These projects will be reviewed by DFS for inclusion in the program. Center scientists may serve as project leads. Center scientists provide technical guidance, method documents and validation protocols as requested by ORA scientists and DFS for projects included in the method development and validation program.

6.5 ORA Method Development and Validation Process

6.5.1 Laboratory Method Development and Validation Program (MDVP) Overview

The MDVP program supports five project categories:

Method Development

- Projects are designed to develop and implement new methods.

- Expected Outcome: A new method is implemented within the laboratory or method validation proposal for field wide implementation.

Method Validation

- Projects are designed to evaluate innovator validated methods via peer reviewed assessment and inter-laboratory collaborations.

- Expected Outcome: Validated regulatory method for field wide implementation.

Method Modification, Enhancement, and Extension

- Projects are designed to extend an existing method to one or more additional matrices or analytes; projects designed to improve an existing method.

- Expected Outcome: Modified method implemented within the laboratory or method validation proposal for field wide implementation.

Technology Exploration

- Projects are designed to investigate and evaluate the usefulness and applicability of new technologies and increase our base expertise in these new technologies.

- Expected Outcome: New technology accepted by one or more publications summarizing experiments performed, data collected, and recommendations.

Applied Studies

- Projects are designed to test hypotheses related to FDA mission such as food safety, quality mechanisms, contaminants, analyte/matrix interactions, metabolism studies, degradation/depletion studies, process effects, stability studies. Although method development may be a component of these projects, it is not the primary focus.

- Expected Outcome: Study, results, and impact for FDA described in one or more publications.

The MDVP process is designed to increase flexibility and timely planning of quality projects that benefit the agency. Each ORA laboratory is required to have an ongoing MVDP plan commensurate with their method development and validation time allotment. A good program is mission related and does not duplicate research work being done elsewhere.

Laboratory management, analysts, and Science Advisors have an important role in managing the program. Throughout the year, method development and validation progress and accomplishments are

monitored and adjustments made to react to emerging analytical needs as they arise. Laboratories are expected to fully plan and accomplish their assigned method development and validation time.

6.5.2 Method Development and Validation Program Procedures

6.5.2.1. Call for Proposals

DFS issues a request for proposals to ORA Laboratories and Centers for the highest priority method development and validation projects that target validation, development, and enhancement of regulatory methods. Additionally, at that time, laboratories may submit proposals for projects not listed in the call for proposals to be considered for future program needs.

The call for proposals issues semiannully with approximately a thirty (30) day deadline for proposal submission.

6.5.2.2 Proposal Preparation and Submission

The Division of Field Science MDVP Call for Proposals issues semiannually and includes the following information:

- a list of method development and validation projects requested for study; and
- Method Development and Validation Program Record.

1. Method Development and Validation Project Record (MDVP record)

See Appendix I

A Method Development and Validation Project Record (Proposal Form) is completed by the laboratory personnel for those projects requested from DFS.

a. An MDVP proposal shall include the following information:
   - project number;
   - title;
   - estimated number of hours or timeline;
   - purpose;
   - describe the problem the project intends to solve;
   - regulatory significance and relevance to the FDA mission;
   - literature search and supporting documents;
   - current issues and recent accomplishments in the field;
   - experimental plan/methods and materials

- describe in detail the experimental approach, methods and materials
- QC/QA controls, validation/extension protocol requirements from the appropriate source (e.g. Laboratory Manual, Volume II, ORA-LAB5.4.5, AOAC, BAM, CVM protocol, CFSAN/DFS microbiology protocol);

- anticipated results
  - future plans (e.g. collaborative study, publications);
- safety requirements;
- budget
  - funding requirements and declaration of funding support; and
- appropriate signatures and endorsement.

b. Additional information applicable to the following studies shall be included in the MDVP project record:

Method validation studies

- method validation protocol (e.g. single lab validation, collaborative study)

Method Modification, Enhancement, or Extension

- method description;
- technical details of the modification; and
- benefits of the modification.

Continuing Projects

- identify the accomplishments from the previous project;
- propose a new plan of work or update Experimental Plan/Methods and Materials; and
- update literature review.

All MDVP proposals are sent to the Division of Field Science; the contact DFS representative is defined in the DFS Call for Proposals.

- signatures and endorsement.

6.5.2.3 Proposal Review and Project Assignment

Proposals are submitted to DFS. DFS performs the review internally and/or assigns the review to a scientist/science advisor in the Center with expertise in the technology area. Within 30 days of submission a meeting will be held with DFS and science reviewers to determine proper method pathway to follow. The project will either be recommended for the "MDVP Committee Pathway" or the "DFS Research Pathway" (Appendix III)

Proposal review considers, but is not limited to, scientific merit (e.g. objectives are realistic and scientifically sound), mission importance, FDA impact, literature background, budget, timeframe, accuracy completeness of the submission, and likelihood of success.

Assignments will be based on review, FTE distribution, and availability of hours. A Research Project Number (RPN) number, assigned by DFS, is used by the analysts to track their time in FACTS.

Because laboratories have specific capabilities and programs, resources will not be limited to only the high priority projects. Low priority projects will be considered if high and medium priority projects are addressed and resources are still available.

6.5.2.4 Regulatory Pathway Approval

After proposals are received, DFS will organize a meeting with the appropriate Center review scientists to discuss each project. This MDVP Review Committee will review each proposal and will either recommend the proposal for one of two pre-defined pathways (the Regulatory Pathway or Non-Regulatory Pathway), or the proposal will be rejected with comments to the investigators.

If the MDVP Review Committee concludes that the project is appropriate for the Regulatory Pathway, the committee will notify the laboratory of its decision. The proposal will either be approved as written or approved with minor revisions. The MDVP Coordinator will grant the proposal research hours and the laboratory will move forward with the accepted project.

Once the project is completed, the data and conclusions will be presented to DFS for final evaluation. DFS will then decide weather to approve the project for validation, or disapprove it pending further research. If disapproved, the researchers can propose further research or discontinue the project.

If approved for validation, DFS will coordinate with the Centers to validate the method according to a recommended validation level, if applicable (see ORA-LAB.7 for Qualititative Microbiology Methods Validation). After the method is validated at the appropriate DFS recommended level, the method should be submitted for inclusion into a regulatory compendium (i.e AOAC), an approved FDA compliance program, or peer reviewed journal. If a method fails validation, it may be determined not fit for use and terminated or re-proposed for validation by the principle investigators.

6.5.2.5 Non-Regulatory Pathway Approval

If the MDVP Review Committee concludes that the proposal is not appropriate for the Regulatory Pathway, DFS will decide whether the proposal is appropriate for the Non-Regulatory Pathway. DFS will review the proposal to determine its value as a non-regulatory method such as for use as a laboratory screening tool. If DFS determines there is no value in this proposal as a non-regulatory method, the proposal will not be approved and the laboratory will be notified why.

If DFS does determine there is value in the project as a non-regulatory method, the MDVP Coordinator will send the laboratory a review decision as approved or approved with minor revisions. The MDVP Coordinator will grant the proposal research hours and the laboratory will move forward with the accepted project. Once the laboratory completes the research, they will present their data and conclusions to DFS for final evaluation.

DFS will then review the data and conclusions and decide if the project is fit for non-regulatory use. If DFS concludes that the project is not fit for non-regulatory use, the laboratory will be notified that further research is necessary. If DFS does conclude that the project is appropriate for non-regulatory use, DFS and the laboratory will again present the project, along with the new data and conclusions, to the MDVP Review Committee for inclusion into the Regulatory Pathway.

If the MDVP Review Committee concludes that the project is now appropriate for the Regulatory Pathway, the project will proceed down this pathway (see Section 6.5.2.4) at the point of method validation. If the MDVP Review Committee concludes that the project is still not appropriate for the Regulatory Pathway, the laboratory should proceed with publication of the project in a peer-reviewed journal or as a Laboratory Information Bulletin (LIB).

6.5.2.6 Project Execution and Reporting

Projects are managed and executed at the laboratory.

Accurate and timely reporting is provided through FACTS.

- report hours under the Miscellaneous Operation Screen.
- FACTS instructions
    1. select Navigate
    2. select Miscellaneous Accomplishment Hours
    3. select Create
    4. enter Research Operation Code: 01
    5. enter accomplishment dates, district
    6. enter Reference Number: Research Project Number (if applicable)
    7. enter Description: "RPN #######, project title"
    8. enter name, hours, applicable PAC code

The recommended timeline and schedule for project completion is:

≤ 500 hours = 6 months
> 500 hours = 12 months

Upon project completion, a final project report, a Laboratory Information Bulletin or article for a peer-reviewed journal is submitted to DFS summarizing results and conclusions.

See Appendix C, Laboratory Information Bulletin for guidelines.

The project status is provided to DFS by laboratory management on a quarterly basis and maintained in a database by the DFS Coordinator. Project updates may be provided by telecom, written report, or by Webex Seminar depending upon the amount of progress that has been made and the current status of the project. The report will also be updated to include regulatory impact, publications, presentations, collaborative studies, adoption as official methods (adoption by other field and headquarters laboratories), and inclusion in compliance programs. The report also assists both the laboratory managers and DFS with future planning.

6.5.2.7 Presentation, Assessment, and Implementation

The basic product of scientific research is information. Dissemination of information ensures others interested in the problem can use the data. To accomplish this, ORA encourages and supports several types of research products.

Scientific Articles

All MDVP outcomes, at a minimum, should be published as a Laboratory Information Bulletin (LIB), or preferably published in a peer-reviewed journal. Manuscripts for outside publications must be reviewed and approved for technical correctness and adhere to Agency and ORA policy and guidance on review and clearance. See Section 6.6.

Authors are expected to produce manuscripts that are coherent, scientifically sound, and likely to be accepted for publication.

Local management is responsible for funding and ordering reprints. Manuscripts intended for publication as an LIB must be reviewed and approved by the Science Advisor, Laboratory Director, and District Director before submission to DFS.

Results may be presented at scientific meetings as lectures or audio-visual sessions. Review and clearance of the presentations is in accordance with Agency and ORA policy. See section 6.6.

If the intellectual property produced by authors has potential for patent application or licensing, the Laboratory Director should submit PHS Employee Invention Form (PHS-6364) with other supporting materials to CRADA for further evaluation. Any publication submission including LIB will be withheld pending the CRADA decision.

Studies

Some studies will become basis for new projects (e.g. new methods go on to validation studies) and be listed in the next call for proposals

After the study initiator has performed ruggedness testing or intra-laboratory collaboration to ensure that a method is likely to succeed in a full-scale study, a request, accompanied by the method and collaborative study protocol, is sent to DFS to select collaborators for the study. DFS will review the proposed study for suitability of the method and clarity of the directions as stated in the protocol. DFS issues the call for collaborators and informs the initiator of those who agree to participate. In an AOAC collaborative procedure, the initiator must obtain approval from local management before requesting Associate Referee status from the appropriate AOAC General Referee.

Assessment and Implementation

DFS, in conjunction the appropriate Center or headquarter offices, and with ORA laboratory management input, can determine how methods are to be implemented. Methods can be implemented through compliance programs, FERN tests, and assignments. New or improved methods, validated methods, adoption of new technology or rapid methods can be implemented field wide.

6.6 Scientific Conduct[1] When Performing Research

ORA analysts are responsible for adhering to the highest standards of intellectual honesty and ethical standards when formulating (MDVP proposals), conducting or presenting method development/validation, studies or research. ORA scientists are expected to follow the guidelines below. The guidelines promote uniform application of the highest ethical standards when conducting research. Violation of these guidelines can undermine the supervisor's trust in the employee as well as the reader's trust of the author's work which in turn undermines the public's trust in the Agency.

6.6.1 Data Management[1]

Data from analysis, studies, instrument data, and statistical data is recorded with integrity and is inseparable from the acquisition.

All data generated is documented and recorded directly, promptly and, if not computer generated, legibly.

All data is retained by the analyst to allow analysis and repetition by others. The schedule for retention is included in the local laboratory's procedure or in the SMG 3291.2, Field Office Filing System.

6.6.2 Publication Practices

Publication is an integral and essential component of method development/validation, studies or research.

Authors are responsible to produce an official publication that is accurate, well written, reflect the Agency's position, and do not disclose trade secrets, confidential commercial information, or other non-public information.

Timely publication of new significant results is important for the progress of science, but fragmentary publication of the results of a scientific investigation or multiple publications of the same or similar data are inappropriate.

All information that would be necessary for scientific peers of the author(s) to repeat the study should be in each paper or made available from the author/s.

Check the referenced sources - It is the Analyst's responsibility to ensure that the scientific article is accurate, carefully researched and referenced.

Plagiarism of any kind will not be tolerated. In general terms, plagiarism[2] is the act of representing someone else's words or ideas as one's own without crediting the true source or origin.

6.6.3 Review and Clearance Policy

All ORA laboratory managers, supervisors, and analysts follow current FDA and local policy and procedures for review and clearance of scientific articles. Scientific articles are defined as the following: publications, articles, speeches, presentations and Laboratory Information Bulletins (LIB).

FDA has a policy[2] stating that scientific articles are reviewed for the following: scientific and technical accuracy; agreement with current Agency policy or future regulatory programs; and not adversely affecting the requirements of policies on other FDA centers or offices.

All scientific articles should be peer reviewed prior to submitting for review and clearance.

It is the responsibility of the author's to make revisions and corrections deemed necessary by their supervisors during the clearance process.

If appropriate, add a disclaimer to the scientific article. The FDA policy [2] defines when a disclaimer is necessary.

6.6.4 Authorship

Authorship refers to the listing of participating scientists' names in all communications, oral and written, experimental results and their interpretation to scientific colleagues.

Authorship is based on significant contributions to the conceptualization, design, execution or interpretation of a research study.

For those individuals who have limited contributions to a study, e.g. providing certain advice, reagents, analyses and support, these individuals may more appropriately acknowledged but not listed as authors.

References:

1. U.S. Department of Health and Human Services, PHS, Guidelines for the Conduct of Research within the Public Health Service, January 1, 1992

2. FDA Policy on the Review and Clearance of Articles to be Published in Scientific or Professional Journals (available at http://intranet.nctr.fda.gov/documents/FDAPublicationPolicy.pdf)

6.7 Document/Change History

Version 1.2	Revision	Approved: 06/23/05	Author: LMEB	Approver: LMEB
Version 2.0	Revision	Approved: 12/06/06	Author: LMEB	Approver: LMEB
Version 2.1	Revision	Approved: 06/06/08	Author: LMEB	Approver: LMEB
Version 2.2.	Revision	Approved: 08/15/08	Author: DFS	Approver: LMEB
Version 2.3	Revision	Approved:12/ 03/08	Author: DFS	Approver: LMEB

Version 2.0 changes:
Chapter underwent major revision to reflect the current Method Development and Validation Program.

Version 2.1 changes:
6.5.2.2 and 6.5.2.3 – Calls for Proposals changed from quarterly to semiannually.
Reference 2. changed to the accessible policy on publication.

Version 2.2. changes:
Table of Contents – 6.5.2.1-6.5.2.7 revised
Appendix III – added
6.4.3 – added "the Centers" to second paragraph
6.5.2.1- 6.5.2.7 - revised
6.5.2.6 – revised sixth paragraph

Version 2.3. changes:
6.3.2 – inserted "in" after described
6.5.1. Technology Exploration – changed implemented to accepted
6.5.2.3 – added (Appendix III) at end of first paragraph
6.5.2.4 – updated SOP information in fourth paragraph
6.5.2.5 Scientific Articles – added last paragraph

APPENDIX I: Method Development and Validation Project Record

<table>
<tr><td colspan="3">METHOD DEVELOPMENT and VALIDATION PROJECT RECORD</td><td colspan="3">1. PROJECT NUMBER</td></tr>
<tr><td colspan="3" rowspan="2">5. TITLE</td><td colspan="3">2. LABORATORY</td></tr>
<tr><td colspan="3">3. FISCAL YEAR(S)</td></tr>
<tr><td colspan="3"></td><td colspan="3">4. RPN NUMBER</td></tr>
<tr><td>6. SCIENTIST(S),
NAME, SIGNATURE
AND DATE</td><td colspan="5"></td></tr>
<tr><td colspan="2">7. CONTINUING RESEARCH</td><td>8. PROJECT PLAN</td><td colspan="2">9. TIME</td><td></td></tr>
<tr><td colspan="2" rowspan="3">☐ YES (If yes explain in item 10)
☐ NO</td><td rowspan="2">STARTING DATE</td><td>FISCAL YEAR</td><td>HOURS</td></tr>
<tr><td></td><td></td></tr>
<tr><td rowspan="2">COMPLETION DATE</td><td></td><td></td></tr>
<tr><td colspan="2">TOTAL HOURS</td><td></td></tr>
<tr><td colspan="6">10. COMMENTS</td></tr>
<tr><td colspan="2">11. NAME OF SCIENCE ADVISOR (Date)</td><td colspan="2">12. NAME OF SUPERVISOR (Date)</td><td colspan="2">13. NAME OF APPROVING SUPERVISOR</td></tr>
</table>

APPENDIX II: Laboratory Information Bulletin Format

Title

Author(s)/Affiliation- The main contact for the work should be identified by an asterisk or number. An e-mail address or phone # for the main author should be provided. In case the authorship includes Non-FDA persons, a consent letter (e-mail) from that author would be appropriate.

Abstract- An abstract should provide a condensed version of the method, describing the major concerns and scope of the article. This should be about one paragraph long.

The special **ADMINSTRTION NOTE** must be added on the first page of every Laboratory Information Bulletin (LIB).

The Laboratory Information Bulletin is a tool for the rapid dissemination of laboratory methods (or information) which appear to work. It may not report completed scientific work. The user must assure him/her by appropriate calibration procedures that LIB methods and techniques are reliable and accurate for his/her intended use. Reference to any commercial materials, equipment, or process does not in any way constitute approval, endorsement, or recommendation by the Food and Drug Administration.

Since LIBs will be submitted electronically and posted on the DFS web site they need to be 508c compliant.

Section 508c of the Rehabilitation Act of 1978 as amended: Section 508 (508 statute html, 508 statute pdf) requires that Federal agencies' electronic and information technology is accessible to people with disabilities, including employees and members of the public.

Section 508 establishes requirements for any electronic and information technology developed, maintained, procured, or used by the Federal government. The term "electronic and information technology" has been defined by the Access Board in regulations published December 21, 2000. Section 508 exempts national security systems from its requirements.

Information regarding all aspects of assistive technologies and accessibility under Section 508 is available at the federal government's official website, http://www.section508.gov/.

This includes charts, figures, tables, pictures, text, hyper links.

Introduction- This should be approximately one or two paragraphs providing background information on FDA's concern and interest into the development of this method/method change.

Experimental- Although this section should be as complete as possible, author(s) should be careful about product and manufacturer names. For example, under method development we may use commercial kits and compare kits from multiple manufacturers. Some of these kits may be regulated

products. The data may suggest that a kit does not meet labeling claims or one kit is better than the competitors. LIBs are reports of experimental data. They are not the route for taking regulatory action. Action cannot be taken, because the method is not official; that is, under development. We cannot set policy through LIBs. This would also be true when developing methodology to determine the effectiveness of products. The author(s) should code the reagent/equipment. Author(s) should also identify any deviations if the product is not used as labeled. Deviations can impact limits of detection, limits of quantitative, linearity, ruggedness.

Use of official samples should be avoided as much as possible. In case we need to use official samples, bacterial isolate, care should be adopted to remove original number/designation to protect confidentiality.

This area should be divided into the following basic areas:

Equipment- list of all equipment to perform the method and sources
Reagents- list of all reagents used in the method and sources
Procedures:
Instrument Parameters– provide wavelengths, temperatures
Standard Preparations- describe dilution schemes
Sample Preparations- describe extractions, spiking, special handling and dilutions
Data-provide charts or graphics of the data collected from the experimentation. Summary data can be provided depending on the amount of data collected. Presentation should be concise to make interpretation easy to view.
Statistical Evaluation – author(s) should identify the statistical method, the null hypothesis, the planned comparisons, unplanned comparisons, and the acceptance level. Unplanned comparisons lose a degree of freedom. The number of replicates need to obtain the statistical power should be predetermined.

Results and Discussion-This can be several paragraphs discussing the conclusions that can be drawn from the data presented. The last paragraph should contain a short summary of the findings.

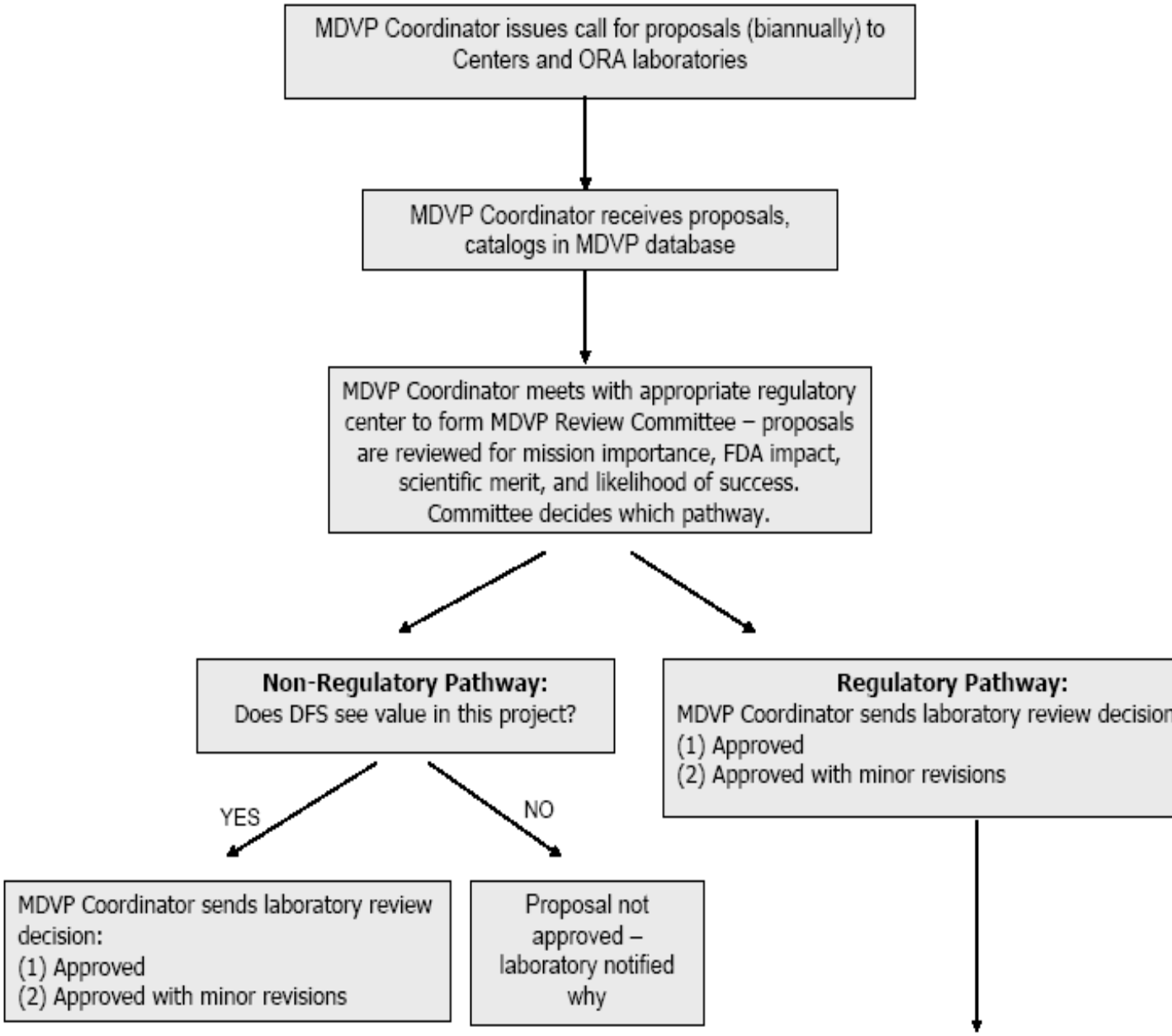
Acknowledgments: This area provides the author(s) an opportunity to thank persons who assisted in the research of the project. This could also include review, grants, outside funding.

References: This is a listing of any articles, books, that were used by the author(s) as a source of information presented but not developed during the project. References should be listed numerically in order of appearance in the LIB. References should include author(s), title, year, journal/book, volume/edition and first and last pages. In press, submitted for publication and personnel communications should be identified and reported as such.

Other comments:

- In case of microbiological identification on chromogenic agar/media, the authors need to understand that the LIB is published on yellow paper and colors will not be able to be distinguished. Possibly by 2006 the web programs will be able to handle some of these concerns.
- For microbiology/molecular biology related work nomenclatures, abbreviations may follow ASM guide lines. Specific instructions are easily available in www.ASM.org. This site can also provide some guidelines about tables, graphs.
- Standard abbreviations (e.g., AOAC) can also be used, but the authors should site/identify the source. Nonstandard abbreviations that do not have an identified source should be defined at first use.
- LIBs are currently not searchable on the web applications, but improvements are being addressed to include these capabilities in 2006.
- List of key words

APPENDIX III: MDVP FLowchart



APPENDIX III: MDVP Flowchart