VOLUME I

LABORATORY MANUAL
Of
Quality Policies

FOR

ORA Regulatory Laboratories

Division of Field Science
Office of Regulatory Affairs
Food and Drug Administration

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1.0 Introduction

This Office of Regulatory Affairs (ORA) Laboratory Manual of Quality Policies (hereafter referred to as Volume I) has been prepared to meet the requirements for laboratory accreditation of the International Organization for Standardization/International Electrotechnical Commission (ISO/IEC) 17025 (2005). It has been formatted using clause numbers from ISO/IEC 17025 to provide ease in review.

2.0 Controlled Distribution of the Quality Manual

The Division of Field Science (DFS) is responsible for maintaining the official master copy of the ORA Laboratory Manual which contains the ORA Quality Manual. The ORA Quality Manual consists of Volume I, ORA Laboratory Manual of Quality Policies and Volume II, ISO 17025 ORA Laboratory Procedures. General distribution of this manual is accomplished using a computer network. Annual review is coordinated by the Division of Field Science.

3.0 Quality Policy Statement

ORA laboratories are committed to laboratory accreditation according to the requirements of ISO/IEC 17025. This commitment is evidenced by the approval signatures for this manual.

The quality policy statement is stated in Volume I, Subsection 4.2.2

4.0 Management Requirements

4.1 Organization

I. Principal Responsibilities

The Associate Commissioner for Regulatory Affairs (ACRA) is responsible for establishing the organization's commitment to the management system, implementing it, and delegating responsibility for its accomplishment.

The Director of the Division of Field Science is responsible for issuing policy and procedures for the ORA laboratories and monitoring their implementation.

Laboratory management, including supervisory analysts and quality managers, is responsible for ensuring that analytical activities meet the requirements of the agency, its customers, and

regulations in 21 Code of Federal Regulations (CFR), 29 CFR, Part 1910.1450, 40 CFR, Parts 260-264, 49 CFR, Parts 171-173 and the Food, Drug and Cosmetic (FD&C) Act. In addition, each person involved in the generation of data is part of the management system.

II. Policies

4.1.1 The Food and Drug Administration (FDA) is a government agency under the Department of Health and Human Services (HHS). The agency is required to follow the federal regulations in 21 CFR, 29 CFR, 40 CFR, 49 CFR, the FD&C Act and PHS Act.

4.1.2 The intent of ORA is to operate testing laboratories according to the following requirements:

- FDA policies and procedures,
- ISO/IEC 17025,
- customer contracts (workplan),
- ORA compliance programs and assignments,
- Federal and State laws and regulations, and
- American Association of Laboratory Accreditation (A2LA) Accreditation Criteria.

4.1.3 ORA laboratories operate permanent facilities in five regions across the United States and Puerto Rico at the addresses identified in the Staff Manual Guide (SMG), Section 1300. ORA may operate mobile laboratories as extensions to specified fixed laboratory sites.

4.1.4 The regulatory laboratories are a part of the Office of Regulatory Affairs, FDA and are identified in the SMG, Section 1300. The organizational charts are found at www.fda.gov and www.dhhs.gov. Each laboratory also maintains an organizational chart or charts. Key personnel are identified in these charts.

4.1.5 a. The laboratory has managerial staff with the authority to discharge their duties as reflected in the prepared job descriptions by the laboratory. This authority includes the implementation, maintenance, and improvement of the management system. Management authorities are defined in government classification standards found in the Qualifications Standards for General Schedule Positions Operating Manual (X-118). The resources needed to discharge these duties are identified in Volume I Section 5.2 to Section 5.6. The identification of departures from the management system and testing requirements is documented according to the laboratory's corrective action procedure.

4.1.5 b. A Financial Disclosure form OGE 450 is completed annually by employees to prevent participation in any financial matter that might adversely affect the integrity of their work. Form HHS 520, Approval of Outside Activity, is completed and approved for employees seeking outside employment.

4.1.5 c. Reports of information and data are transmitted and filed in accordance with official policies, directives, and notices of the department and the agency. Reports and data are not released until reviewed and verified. The majority of reports are sent to internal customers only, except as required by law or regulation. Information is released only to the customer or designated representative. Field Management Directive (FMD) No. 147, Procedure for Release of Analytical Results Pursuant to Section 704 (d), provides guidance for reporting analytical results to an external customer. Additionally, FDA facilities are controlled-access buildings to further ensure protection of data.

4.1.5 d. To avoid conflicts of interest, pressures, and influences, FDA employees are familiar with and observe the Standards of Ethical Conduct. These principles of ethics can be found at http://www.fda.gov/opacom/ethics/default.htm. Executive Order 12674, issued in 1989 and modified in 1990 by Executive Order 12731, states fourteen general principles that broadly define the obligations of public service. Two core concepts are embodied in these principles: (a) Employees shall not use public office for private gain, (b) and employees shall act impartially and not give preferential treatment to any private organization or individual. The Office of Government Ethics (OGE) requires one hour of ethics training annually. Training is provided on ethics rules, regulations and integrity in order to help employees avoid placing themselves in a conflict of interest situation. An employee who performs laboratory testing performs and documents a demonstration of competence as prescribed in Volume I, Subsection 5.2

4.1.5 e. The regulatory laboratories are a part of the Office of Regulatory Affairs, FDA and are identified in SMG, Section 1300. The organization and the relationship among the laboratory staff is reflected in the laboratory's organizational chart maintained by the laboratory Quality Management System (QMS) Manager.

4.1.5 f. Job responsibilities for laboratory employees are documented in the management system procedures and operating instructions. Position descriptions are maintained by the laboratory.

4.1.5 g. The laboratory employees performing testing have access to consensus standards, instrument manufacturers' manuals, and laboratory procedures for reference.

Demonstration of competence for technical personnel is documented and used as evidence of desired familiarity with laboratory methods. Supervisors are designated and trainees do not perform regulatory work until competent as per the laboratory training program.

4.1.5 h. The Supervisor is responsible for the technical operations of the laboratory. Resources for training, laboratory methods, measurement traceability, and purchasing are described in sections of this Volume, and in procedures.

4.1.5 i. The laboratory Quality System Manager (QSM) is responsible for the laboratory's management system and its implementation. The QSM has direct access to the Laboratory Director, who is responsible for decisions concerning policy and resources.

4.1.5 j. Qualified laboratory personnel are assigned to serve in the absence of key managerial personnel, such as Laboratory Director, Quality System Manager, and Supervisor. For example, the Supervisor or Deputy Director may serve in the absence of the Laboratory Director; either the Laboratory Director, Deputy Director or Supervisor may serve in the absence of the QSM; and senior technical personnel may serve in the absence of Supervisors.

4.1.5 k. Laboratory personnel are aware of their function and contribution in the management system and of its objectives.

4.1.6 Effective communication from management occurs through the use of but not limited to memos, newsletters, electronic presentations, emails, or verbally to laboratory personnel regarding the effectiveness of the management system.

Related Procedures

- The Qualifications Standards for General Schedule Positions Operating Manual (X-118)
- Each ORA laboratory has its own corrective action procedure. A template is provided in Volume II, Section 1, ORA-LAB.4.11 Corrective Action Procedure.
- Each ORA laboratory has its own training procedure. A template is provided in Volume II, Section 1, ORA-LAB.5.2 Personnel: Training Procedure.

4.2 Management System

4.2.1 The laboratory management system is outlined in the following documents:

- Quality manual,
- Written procedures,
- Work Instructions,
- References, and
- Forms and records.

This management system is established to address the requirements in ISO/IEC 17025. Each entity establishes and maintains a master list of procedures per the procedure for document control. The quality policy and quality objectives for ORA laboratories are included in Volume 1, subsection 4.2.2. The documents listed above are accessible to all personnel and are included in the laboratory's training program.

4.2.2 Management System Policy

Mission

ORA's mission statement states "ORA protects consumers and enhances public health by maximizing compliance of FDA regulated products and minimizing risk associated with those products". FDA laboratories are committed to providing testing that meets both the needs of the customers and the requirements of ISO/IEC 17025 and to continually improve the effectiveness of the management system. Testing results are reported within stated limits of accuracy, precision, and detection limits as described in the methods used for analysis.

Commitments to Quality Issued by Director, Division of Field Science

4.2.2 a. Good Professional Practice and the Quality of Testing

ORA laboratories are committed to the Standards of Ethical Conduct which define the obligations of public service issued under Executive Order 12674. Testing is conducted according to the policies stated in Volume I, subsections 5.4**;** 5.7. The laboratory management and personnel are committed to performing quality activities to assure integrity, accuracy, precision, reliability and timeliness of the data.

4.2.2. b. Standard of Service

The laboratory's standard of service for the testing program is defined by the ISO/IEC 17025 requirements, FDA regulatory needs included as part of the laboratory methods, and the following:

- Established and maintained documented procedures for laboratory operation based upon consensus methods for testing. Methods are specified or cited in the compliance program and compendiums, or by the customer. In some cases, testing and procedures as established by the instrument manufacturer are used.

- Sample handling and management procedures to maintain integrity of both the samples and the documentation to support the analytical data.

- Maintenance of records in such manner that facilitates retrieving them later. Records are maintained in the analyst worksheet packet filed by sample number. Records may be archived on- or off-site depending on the home district of the collector. Archival retention periods are stated in the laboratory's document control and management procedure.

- Employment of qualified and trained personnel to perform the tasks to support the laboratory objectives. Performance demonstrations by technical personnel conducting laboratory methods are conducted and documented.

- Routine maintenance of quality control data to support testing results by demonstrating that measurement processes are maintained in statistical control. Accuracy and precision control charts are used to monitor performance.

- Maintenance of an instrument calibration program that provides measurement traceability to International System of Units (SI) units. This is accomplished with the use of national, international, or industry accepted standards of measurement.

ORA laboratory personnel follow the policies included in this Volume, the processes described in their local operating procedures, and the processes described in laboratory methods referenced in this Volume.

Changes to management system documents are made according to the laboratory document control procedure and involve periodic revisions of this Volume as part of the annual management review of the management system.

An internal audit process is used to evaluate the effectiveness of the management system established for laboratory operations. It is the policy of ORA laboratories to participate in interlaboratory proficiency programs as these are announced and as requested by the accrediting body.
The sections in this Volume describe elements and reference procedures that outline the management system established to accomplish the mission of the laboratory.

Test reports and the communication of information generated by the laboratory are conducted under the direction of the Laboratory Director.

The operational procedures for the laboratory are listed in its master list**,** as described in the laboratory's document control procedure**.**

4.2.2 c. Management System Objectives

The primary objective of the management system established by ORA laboratories is to assure the accuracy and precision of laboratory results so that they will be reliable, interpretable, repeatable, and defensible. Data quality objectives are described in the terms of:

- accuracy,
- precision,
- detection and quantitation limits,
- timeliness, and
- comparability.

The second objective is to establish and maintain national and international recognition through compatibility with the requirements of relevant standards.

Third, strive to meet or exceed the customer's needs and expectations for precision, accuracy, sensitivity, and specificity.

Fourth, maintain ORA laboratories' reputation for quality by fostering continuous process improvement and problem prevention.

These objectives are taken into account as part of the reviews performed by management.

4.2.2 d. Management System Awareness and Implementation

The management system documents and test methods are included as training elements in the laboratory's training program addressed in the laboratory training procedure. This ensures that staff is familiar with quality documentation and implement the quality policies and procedures in their work. See template, Volume II, Section 2, ORA-LAB.5.2 Personnel: Training Procedure.

The implementation of the quality policies is evidenced by the manner in which work activities are conducted. Implementation of the management system procedures is evidenced by the generation of required records. The audit and management review activities are the mechanisms that are used to monitor the implementation effort of the laboratory management system.

4.2.2 e. Commitment to ISO/IEC 17025.

The policies for operation of the laboratory management system are established to address the requirements of ISO/IEC 17025. ORA laboratories are committed to laboratory accreditation according to the requirements of ISO/IEC 17025. This commitment is evident by the approval signatures by each Laboratory Director for this quality manual.

4.2.3 Evidence of management's commitment to the management system and its continual improvement in effectiveness is demonstrated by but not limited to participation of managers in the management reviews, performance of internal audits, proficiency testing, and the analysis of quality control samples.

4.2.4 Effective communication from management occurs through the use of but not limited to memos, newsletters, electronic presentations, emails, or verbally to laboratory personnel regarding the importance of meeting customer, statutory, and regulatory requirements.

4.2.5 Procedures and Outline of the Management System

Management system procedures supporting quality policies are cited in the Related Procedures at the end of each section of this Volume. The outline of the management system is included in Volume I, Subsection 4.2.1. Where needed, each laboratory shall have procedures to implement the quality policies at the local level and include these procedures in its Master List. Laboratories shall include a reference to the corresponding requirements in this Volume.

4.2.6 Roles and Responsibilities

General roles and responsibilities for ORA laboratory personnel are summarized as follows:

- Quality System Manager
  - Ensures that the management system is established, implemented, and maintained in conformance with the requirements of ISO/IEC 17025.
  - Advocates and coordinates quality improvements to the management system.

- Responsible Managers (technical management)
  - Oversee technical functions.
  - Ensure compliance with the requirements of ISO/IEC 17025.
  - Ensure management system procedures, applicable standards, specifications, and regulations are followed.
  - Ensure that qualified, skilled, and trained personnel and other resources are available.
  - Ensure that products and services satisfy customer requirements.

- Analysts
  - Ensure the quality of their work.
  - Operate in conformance with the requirements of the management system.

4.2.7 The management system process and procedures as defined in this manual maintain the integrity of the management system when changes such as a change in the structure of the organization or management, or a change is a policy or procedure are made.

4.3 Document Control

4.3.1 General

The document control and management procedure in each laboratory describes the process for controlling quality documents that form part of its management system. The quality documents include those required for the generation of laboratory data. These documents include those published by the laboratory and those published externally. Documents of external origin include regulations, standards, test methods, instructions and manuals.

4.3.2 Document Approval and Issue

4.3.2.1 Documents issued to personnel in the laboratory as part of the management system are reviewed and approved for use prior to issue in accordance with the laboratory's document control and management procedure. The laboratory's master list identifies the current revision status and distribution of documents in the management system. Through the use of the master list, quality documents are posted to personnel to preclude the use of invalid or obsolete documents.

4.3.2.2 Procedure Content

The laboratory's master list and document control and record management procedure provide for the following:

a. Authorized management system documents and external documents are at locations where operations essential to the effective functioning of the laboratory are performed.

b. Documents are reviewed according to a schedule and revised to ensure continuing suitability and conformance with the management system and ISO/IEC 17025 requirements.

c. Invalid or obsolete documents are promptly removed from all points of issue or use, or marked as *Uncontrolled* to assure against unintended use.

d. Obsolete documents retained for either legal or knowledge preservation purposes are marked as *Archived*.

4.3.2.3 Document Identification

A document control header as described in the laboratory's document control and management procedure uniquely identifies management system documents generated by the laboratory. Such identification includes the date of revision, identification number and inclusive pagination. The issuing authority is indicated by the name of the approving official in the document history section of each document.

4.3.3 Document Changes

Changes to documents are reviewed and approved in accordance with the laboratory's document control and management procedure. Unless designated otherwise, this procedure is followed by

the same personnel or function as in the original review or approval. The use of reference documents and information is required upon which to base the review and approval.

4.3.3.1 The altered or new text is identified either in the document, on a cover page, or in attachments.

4.3.3.2 The laboratory's document control and management procedure addresses the handling of document amendments by hand pending reissue.

4.3.3.3 Computerized Systems

The laboratory's document control and management procedure addresses the control of electronic management system documents.

Related Procedures

- Each ORA laboratory has its own document control and management procedure. A template is provided in Volume II, Section 1, ORA-LAB.4.3., Document Control and Management

4.4 Review of Requests, Tenders and Contracts

4.4.1 Review

ORA, Division of Planning, Evaluation and Management (DPEM) develops and issues the Annual Fiscal Year (FY) Workplan for ORA field units. The portion of the workplan concerned with the laboratories is a cooperative effort among the Centers, ORA Field Committee, and DFS. The workplan is based on several factors such as the budget, the number of analysts and amount of resources, the Commissioner's performance goals, the compliance program accomplishment goals, the inventory of regulated industry maintained by the field units, and FDA-targeted products. Distribution of assignments is by Program Assignment Code (PAC) and full time equivalent (FTE) hours within the different program areas. The compliance programs specify or cite the methods for analyses. The ORA laboratories and DFS review the annual workplan to ensure that each laboratory has the capability and resources to provide the requested services. Any differences between the workplan and the laboratory capability are resolved in accordance with FDA Field Management Directive 17B, Management of Compliance Programs by the Field or through consultation with District/Regional management.

In addition to the workplan, assignments may be issued to ORA laboratories by an ORA headquarters unit or a Center. Multiple district assignments and high priority requests for work are approved according to FDA Field Management Directive 17, ORA Field Assignments-Guidelines for Issuance by Headquarters. Such assignments are cleared through the Office of Regional Operations (ORO). Assignments specify or cite the methods for analyses. Requests not covered by compliance programs or assignments are reviewed prior to receipt of samples by the laboratory's management when possible.

The results of this process are discussed and documented as part of the laboratory's annual management review.

4.4.2 Records of Review

ORA laboratories maintain records of workplan reviews, changes, and change requests (FMD-17B). Records are also maintained of discussions regarding ad hoc assignments.

4.4.3 Subcontracting Laboratories

The policies regarding the use of subcontracting laboratories are found in Volume I Subsection 4.5 Subcontracting of Tests. The customer requesting collaborative testing by laboratories outside of ORA is responsible for the work done by such labs. ORA is not responsible for such work under these circumstances.

4.4.4 Contract Deviations

Requests for deviations from work assignments or compliance programs are processed by the Division of Field Science (DFS). DFS interacts with the customer to determine whether the requested changes are acceptable. Records of contract changes are maintained.

4.4.5 Amendments to Contracts

If a contract needs to be amended after work has commenced, the same contract review process is repeated and any amendments are communicated to all affected personnel named in the contract.

Related Documents

- FDA Field Management Directive 17B, Management of Compliance Programs by the Field

- FDA Field Management Directive 17, ORA Field Assignments-Guidelines for Issuance by Headquarters
- Annual Workplan

4.5 Subcontracting of Tests

ORA laboratories do not subcontract routine analyses within its scope of accreditation. Collaborative activities conducted with external laboratories, such as universities, are research in nature and do not involve the routine analysis of FDA samples.

4.5.1 Subcontracting Laboratories

Based on workload fluctuations and resource needs, ORA laboratories may request samples assigned to other FDA laboratories for analysis. Samples are administratively transferred after arrangements are made to ensure that the receiving laboratory has the capacity and capability to complete it in a timely manner.

Samples are shipped according to Department of Transportation (DOT), United States Post Office (USPS), and carrier regulations. The manual for the Field Accomplishments and Compliance Tracking System (FACTS) describes the procedure for documenting administratively transferred samples (ATS).

4.5.2 Notification of Customer

FACTS, which is accessible to the customer, serves as a notice of the transfer.

4.5.3 Laboratory Responsibility

The FDA laboratory to which the sample has been transferred assumes responsibility to the collector for the work.

Related Procedures

- FACTS Manual

4.6 Purchasing Services and Supplies

4.6.1 Procedure

The laboratory or designated purchasing agents use Federal Acquisition Regulations (FAR) and related procedures for the procurement of materials, supplies and services that critically affect the quality of the tests or calibrations. These procedures describe the process for the selection, purchase, reception and storage of equipment, services and supplies, including reagents and laboratory consumable materials, used in the performance of the tests and calibrations. Each laboratory has work instructions describing the processing of requisitions.

4.6.2 Inspection and Verification

The laboratory's purchasing procedure describes how purchased equipment, supplies, services, reagents, and consumable materials that critically affect the quality of tests or calibrations are inspected or verified prior to use or concurrently with use. Inspection or verification criteria are used to establish conformance with requests made by the customer, included in standard specifications, or defined in the methods.

4.6.3 Purchasing Documents

Purchasing documents for items affecting the quality of laboratory output describe the services or supplies ordered. These purchasing documents are reviewed and approved for technical content prior to submission.

4.6.4 Records and Registry

Records of supplier evaluations and a list of approved suppliers are maintained by purchasers of laboratories equipment, services, and supplies.

Related Procedures

- Government Accounting Office (GAO) Policy and Procedures Manual
- SMG 2610 Procurement and Supply Management
- Federal Acquisition Requirements
- Office of Management and Budget (OMB), General Service Administration (GSA), HHS, Federal Property Management Regulations (FPMR), FDA and ORA manuals, specific issuances

- Public Law (PL) 95-507

Each ORA laboratory has its own purchasing procedure. A template is provided. See Volume II, Section I, ORA-LAB4.6 Purchasing Services and Supplies.

4.7 Service to the Customer

4.7.1 The laboratory affords the requesting customer cooperation to clarify the customer's request within the framework of the contract review process described in Volume I, Section 4.4 Review of Requests, Tenders and Contracts. The laboratory maintains communications regarding deviations from contract work. Communications regarding compliance programs, workplan and assignments are conducted through DFS.

The opportunity for the customer to witness laboratory activity is given upon request, providing the laboratory is able to maintain confidentiality to other customers during such cases.

4.7.2 The laboratory seeks customer feedback on their services and general performance. Records of the comments, both positive and negative, are maintained and are taken into account for identifying management system improvements during the reviews performed by management.

Related Procedures

- None

4.8 Complaints

The laboratory has a complaint procedure describing the process for the receipt and recording of complaints received from any party. Records of all complaints received are maintained according to the procedure. Complaints identified as nonconformities are processed according to Volume I, Section 4.11 Corrective Action.

Related Procedures

- Each ORA laboratory has its own procedure for handling complaints. A template is provided. See Volume II, Section I, ORA-LAB.4.8 Complaints.

4.9 Control of Non-conforming Work

4.9.1 Procedure

The ORA laboratories have a control of non-conforming work procedure that is implemented when any aspect of their testing work, or the results of this work, does not conform to requirements of the management system, testing methods, or the requests of the customer. This procedure addresses the following elements:

- responsibilities and authorities for the management of identified non-conforming work and taking actions such as the halting of work, the withholding of test reports;
- application of criteria to evaluate the significance of non-conforming work;
- remedial action taken, together with any decision about the acceptability of the non-conforming work;
- notification of the customer, and if necessary, recall of work; and
- responsibility for authorizing the resumption of work.

4.9.2 Follow-Up

If the non-conforming work could recur, or there are other significant problems identified, the corrective action procedures in Volume I, Section 4.11 Corrective Action are promptly followed.

Related Procedures

- Each ORA laboratory has a procedure for handling control of non-conforming work. A template is provided. See Volume II, Section 1, ORA-LAB.4.9 Control of Non-conforming Work.

4.10 Improvement

The effectiveness of the laboratory's management system is improved by using the following activities: internal audits; management reviews; analysis of quality control data; corrective actions; preventive actions; the quality policy; and the quality objectives.

4.11 Corrective Action

4.11.1 General

Each ORA laboratory has a corrective action procedure that designates the authorities for implementing corrective action when one of the following is identified:

- non-conforming work,
- departures from the policies and procedures in the management system, and
- departures from required technical operations.

4.11.2 Cause Analysis

The procedure for corrective action includes investigating and determining the root cause of the non-conformance.

4.11.3 Selection and Implementation of Corrective Actions

Potential corrective actions are identified. The action most likely to eliminate the problem and to prevent recurrence is selected.

The corrective action chosen addresses the magnitude of the non-conformance and the risk attributed to the non-conformance.

Corrective actions are documented, and any changes resulted from the corrective action investigation are implemented.

4.11.4 Monitoring of Corrective Actions

The corrective action procedure addresses the monitoring for the effectiveness of corrective actions performed.

4.11.5 Additional Audits

Where the identification of non-conformances or departures casts doubts on the laboratory's conformance with management system policies and procedures or conformance with ISO/IEC 17025, the areas of activity affected by the non-conformance are audited as soon as possible in accordance with Volume I, Section 4.14 Internal Audits.

Related Procedures

- Each ORA laboratory has its own corrective action procedure. A template is provided. See Volume II, Section 1, ORA-LAB.4.11 Corrective Action.

4.12 Preventive Action

4.12.1 General

Sources for needed improvements and potential sources of non-conformance are identified according to the process described in the laboratory's preventive action procedure**,** and are part of the management review process. Preventive actions plans are developed, implemented, and monitored to address the identified opportunities for improvement.

4.12.2 Procedure

The procedure includes the initiation of action. The management review process monitors the effectiveness of such actions in providing improvement to the management system.

Related Procedures

- Each ORA laboratory has a preventive action procedure. A template is provided. See Volume II, Section 1, ORA-LAB.4.12 Preventative Action.

- Each ORA laboratory has a management review procedure. A template is provided. See Volume II, Section 1, ORA-LAB.4.15, Management Review.

4.13 Control of Records

4.13.1 General

4.13.1.1 Procedure

Each ORA laboratory has a control of records procedure for identifying, collecting, indexing, accessing, filing, storing, maintaining, and disposing of quality and technical records. Quality records include reports from internal audits, management reviews, corrective actions, and preventive actions.

4.13.1.2 Legibility, Storage, and Retention

Records are to be legible. Laboratory reports (recorded on FDA form FD-431 and FDA form FD-431a) are archived upon final review to the designated home district office for storage. Laboratory reports can be retrieved by requesting the report from the designated home district record management center. A record retention schedule is included in the laboratory's procedure or in the SMG 3291.2, Field Office Filing System.

4.13.1.3 Security and Confidentially

Access is controlled in FDA facilities; only authorized personnel are allowed in the laboratory and record management center. Records are stored in secured areas. Records are confidential and redacted before release in accordance with Freedom of Information (FOI) process.

4.13.1.4 Electronic Records

Each ORA laboratory has a procedure describing the protection and back-up of electronic records. The procedure also describes the safeguards in place to prevent unauthorized access to or amendment of electronic records.

4.13.2 Technical Records

4.13.2.1 Retained Records, Audit Trail, and Identification

Laboratory reports, depending on the type of analysis, include the original observations, derived data, calculations, standard preparation, instrument printouts, and results. These reports are retained until closed in FACTS and final review is performed. An electronic test report is in FACTS. Staff records, equipment calibration, and verification reports are retained in accordance with the laboratory's control of records procedure.

The records contain sufficient information to establish an audit trail.

The records of each test contain sufficient information in order to repeat the test under conditions as close as possible to the original. This information includes factors that affect uncertainty and any environmental conditions that affect the test.

The collection report in FACTS identifies the personnel responsible for sampling. The FDA form FD-431a includes the identity of the personnel responsible for performance of each test and for checking the results.

4.13.2.2 Recording and Identification

Observations, data, and calculations are recorded at the time they are made and are identifiable to the activity performed. Method numbers and titles are used to provide traceability of records to activities.

4.13.2.3 Corrections

When errors occur in records, each mistake is lined out, not erased, not made illegible, nor deleted. The correct value is entered, initialed, and dated. In the case of records stored electronically, equivalent measures are taken to avoid loss or change of original data.

Related Procedures

- SMG 3291.2, Field Office Filing System
- Food Drug and Cosmetic Act, Section 301(j)
- 18 United States Code (USC) 1905, The Trade Secrets Act
- Each ORA laboratory has its control of records procedure. A template is provided. See Volume II, Section 1, ORA-LAB.4.13 Record and Data Management.

4.14 Internal Audits

4.14.1 General

Internal audits are conducted according to a schedule included in the laboratory's audit procedure. Internal audits are conducted of activities to verify that operations continue to conform to the requirements of the management system and ISO/IEC 17025.

The internal audit program addresses all elements of the management system, including testing activities. The laboratory's Quality Management System Manager is responsible for the coordination of internal audits as listed by the schedule and requested by management.

Trained and qualified personnel are responsible for conducting internal audits. Audits are performed by personnel other than those who performed the work being audited.

4.14.2 Corrective Action

When audit findings cast doubt on the effectiveness of the operations or on the correctness or validity of the laboratory's test results, corrective action is undertaken according to the laboratory's corrective action procedure**.**

The customer is notified if investigations show that non-conformances related to audit results also have affected work performed for the customer. This notification is documented.

4.14.3 Audit Records

The area of activity audited, the audit findings, and corrective action that arise from them are recorded according the laboratory's audit procedure

4.14.4 Follow-up Audit Activities

Follow-up audit activities are conducted to verify and record the implementation and effectiveness of the corrective action taken. This follow-up is included as part of the management review process.

Related Procedures

- Each ORA laboratory has its own audit procedure. A template is provided. See Volume II, Section 1, ORA-LAB.4.14 Audits

- Volume II, Section 1, ORA-LAB.4.11 Corrective Action

4.15 Management Reviews

4.15.1 General

The laboratory's management review procedure includes the schedule for conducting management reviews. This review is conducted by the laboratory's executive management to ensure continuing fitness for use and effectiveness of the management system and to introduce needed changes or improvements.

The management review addresses the elements of the management system and includes but is not limited to the following elements:

- suitability of policies and procedures (Volume II, Section 1, ORA-LAB.4.2 Management System);

- reports from managerial and supervisory personnel (Volume II, Section 1, ORA-LAB.4.1 Organization;
- outcome of recent internal audits (Volume II, Section 1, ORA-LAB.4.14 Audits);
- corrective and preventive actions (Volume II, Section 1, ORA-LAB.4.11 Corrective Action Procedure, 4.11 Preventative Action Procedure);
- assessments by external bodies (Volume II, Section 1, ORA-LAB.4.14 Audits);
- results of interlaboratory comparisons, proficiency test, and quality control (Volume II, Section 2, ORA-LAB.5.9 Assuring the Quality of Test Results);
- changes in the volume and type of work (Volume II, Section 1, ORA-LAB.4.4 Requests, Tenders and Contracts);
- customer feedback (Volume II, Section 1, ORA-LAB.4.8 Complaints);
- complaints (Volume II, Section 1, ORA-LAB.4.8 Complaints); and
- other factors, such as quality control activities, resources (Volume II, Section 1, ORA-LAB.4.1 Organization) and staff training (Volume II, Section 2, ORA-LAB.5.2 Personnel: Training Procedure).

The findings and the actions that arise from the review are recorded according to the laboratory's management review procedure. Each action includes a target date for resolution.

Related Procedures

- Each ORA laboratory has its own management review procedure. A template is provided. See Volume II, Section 1, ORA-LAB.4.15 Management Review.

5.0 Technical Requirements

5.1 General

The sections following below address the factors affecting the correctness and reliability of the tests performed by a laboratory. These factors include contributions from:

- personnel (Volume II, Section 2, ORA-LAB.5.2 Personnel: Training Procedure),
- accommodation and environmental conditions (Volume II, Section 2, ORA-LAB.5.3 Facilities and Environmental Conditions),
- test and calibration methods and method selection and validation (Volume II, Section 2, ORA-LAB.5.4 Test Methods and Validation),
- equipment selection and calibration (Volume II, Section I, ORA-LAB.4.6 Purchasing and Receipt; Section 2, ORA-LAB.5.5 Equipment),
- measurement uncertainty and traceability (Volume II, Section 2, ORA-LAB.5.4 Test Methods and Validation; ORA-LAB.5.6 Measurement Traceability), and
- handling of test and calibration items (Volume II, Section 2, ORA-LAB.5.8 Sample Management).

The procedures listed in each section address these factors.

5.1.2 Contribution to Total Uncertainty of Measurement

These factors are considered in determining total measurement uncertainty and in developing uncertainty budgets. Additionally, these factors are considered by the laboratory when developing test procedures, in the training and qualification of personnel, and in the selection of the equipment utilized.

5.2 Personnel

5.2.1 Personnel Competence

Laboratory management ensures that laboratory personnel have the knowledge, skills, and abilities to perform their duties. Competence is based on education, experience, demonstrated skills, and training. Staff records contain the documentation of personnel education, experience, skills, and training for the position held.

Trainees undergo a training program in accordance with the laboratory's training procedure and FDA Office of Resource Management/Division of Human Resource Development (DHRD) standards. For in-house training, a senior analyst serves as the trainer. Trainees perform procedures when training is completed and competency has been demonstrated. The documented demonstration of competence is an exercise that the trainee performs independent of supervision. The trainee is considered competent after the specified criteria have been successfully met.

5.2.2.1 Goals for Education, Training and Skills

The individual and management are jointly responsible for the setting, the pursuit, and achievement of educational goals for professional advancement. The annual performance evaluation process can be used by the individual to discuss career advancement and training possibilities. By using this process, individuals have the opportunity to identify areas of study and request training oriented towards the attainment of their goals. Procedures for employee career development are described in SMG 3120.1, Staff Development and Training, and FDA Supervisor's Desk Reference, Chapter 8, Training and Development.

Training needs are identified by the analyst's discipline (e.g. Chemist, Microbiologist) and FDA ORM/DHRD standards. In-house training is conducted according to laboratory's training procedure. Present and anticipated tasks of the laboratory are addressed in the planning of special training modules.

Skills of personnel are based upon demonstration of competence. This demonstration is to be completed successfully before analysts generate data independently. The effectiveness of personnel training is documented in but not limited to management reviews, internal audits, external assessments, proficiency testing, and performance evaluations.

5.2.3 Employees and Contracted Personnel

The laboratory utilizes the skills and talent of both full-time employees and contract personnel. The requirements of the management system are administered equally to both categories. No differentiation is made between the two categories of workers. Supervision, training, and competence are documented for all technical and key support personnel.

5.2.4 Job Descriptions

The laboratory maintains active job descriptions for managerial, technical, and key support personnel involved in tests. Job descriptions are established according to The Qualifications Standard for General Schedule Positions Operating Manual (X-118).

5.2.5 Management Authorization

The Laboratory Director authorizes identified personnel to:

- perform testing and calibration,
- issue test reports,
- give opinions and interpretations, and
- operate particular types of equipment.

Records of authorizations, demonstration of competence, education, training, and experience are maintained by the laboratory and dated. Training files are maintained and include these records.

Related Procedures

- Volume II, Section 2, ORA-LAB.5.2 Personnel: Training Procedure
- Each ORA laboratory maintains employee training files and authorizations.

5.3 Accommodation and Environmental Conditions

5.3.1 Facilities and Environmental Conditions

The laboratory environmental conditions facilitate the correct performance of analytical testing. Test methods used by the laboratory include instructions addressing applicable environmental conditions. Examples of environmental influences are energy sources, lighting, biological sterility, dust, humidity, and temperature. The laboratory monitors critical environmental conditions to ensure that results and the quality of the measurement are not adversely affected or invalidated.

In the event mobile labs are deployed, the laboratory is aware of and complies with all the environmental requirements and laws for the location. The technical needs for accommodation and environmental conditions that can affect the results of test are documented with the data generated.

5.3.2 Monitoring

Environmental conditions requiring monitoring include, but are not limited to:

- room temperature and humidity,
- air flow rates for chemical fume hoods,
- biosafety hoods and laminar flow hoods,
- metal contamination on benches and hoods in laboratories performing metal analysis,
- microbiological contamination on bench surfaces and hoods in microbiology laboratories, and
- air sampling for microbiological contamination in microbiology areas.

Where environmental controls are needed, the environmental conditions are recorded.

Testing activities are stopped when the environmental conditions invalidate the test results or adversely affect quality control. Monitoring activities are conducted as part of the laboratory test or calibration methods.

5.3.3 Cross-contamination

Separate areas are maintained for incompatible activities. Measures taken to prevent cross-contamination include but are not limited to:

- chemistry laboratories are separated from microbiology laboratories,
- sample receiving and storage are conducted in designated areas,
- separate storage for standards and reference materials and cultures, and
- microbiology media preparation and sterilization are separated from work areas.

5.3.4 Access

Laboratories are limited access areas. Access is controlled by but is not limited to:

- issuance of keycards for entrance,
- escorting visitors,
- issuance of identification badges, and
- the use of security guards.

5.3.5 Housekeeping

Laboratory areas are maintained clean and orderly to prevent contamination of samples and to facilitate the efficiency of laboratory operations. Volume II, Section 2, ORA-LAB.5.3 Facilities and Environmental Conditions specifies minimum housekeeping measures. The laboratory's Chemical Hygiene Plan and Hazardous Waste Management Plan include measures taken to ensure good housekeeping in the laboratory.

Related Procedures

- Volume II, Section 2, ORA.LAB.5.3, Facilities and Environmental Conditions
- Laboratory Chemical Hygiene Plan
- Laboratory Waste Management Plan

5.4 Test Methods and Method Validation

5.4.1 General

The scope of test technologies and associated method source routinely used are identified in the laboratory's accreditation program documentation.

The estimation of the uncertainty of measurement is addressed in Volume I, subsection 5.4.6. and Volume I, Section 5.9 Assuring the Quality of Test Results of this manual describes the quality control processes, including the application of statistical techniques, for supporting test and calibration data.

The laboratory instructions for the use and operation of equipment called for by the laboratory methods is either a laboratory procedure identified on the master list or as equipment manuals. Procedures for the handling of items for testing are addressed in Volume 1, Section 5.8 Handling of Samples. Equipment manuals and standards for the laboratory's scope of testing technologies are controlled as external documents according to Volume I, Section 4.3 Document Control. Deviations from test methods are documented, technically justified, authorized, and where circumstances call for it, accepted by the customer according to Volume II, Section 2, ORA-LAB.5.10 Reporting Laboratory Data, 6.D.

5.4.2 Selection of Methods

Standard methods are those published by international, regional or national standards-writing bodies; by reputable technical organizations; in legal references; and FDA published methods.

FDA "official" methods are those in compendia specified in the FD&C Act and prescribed in the CFR and methods in applications and petitions that have official status are included. These methods include those in the United States Pharmacopeia, National Formulary, Homeopathic Pharmacopeia of the United States, Official Methods of Analysis of the Association of Official Analytical Chemists (AOAC) International or any supplement of any of them, American Public Health Association (APHA) Compendium of Methods for the Microbiological Examination of Foods, FDA compliance programs, the Pesticide Analytical Manual (PAM), the Food Additives Analytical Manual, the Food Chemicals Codex, FDA Bacteriological Analytical Manual (BAM), FDA Macroanalytical Procedures Manual (MPM), and ORA Laboratory Information Bulletins (LIBs) that are included in compliance programs and special assignments. Standard methods are preferred for use and are verified for use in the laboratory. A standard method may be supplemented with additional details in the form of a laboratory procedure to ensure consistent application. Those methods specified by the manufacturer of the equipment are considered as standard methods.

Laboratory methods are selected to meet the customer's need as addressed in Volume I, Section 4.4 Review of Requests, Tenders and Contracts. The laboratory methods are controlled as external documents according to Volume I, Section 4.3 Document Control.

When the customer does not specify the method to be used, a standard method is preferred for use. If a standard method is not found the laboratory may use either a non-standard method or modify a method for use with the concurrence of the customer. The non-standard or modified method is validated according to Volume I, subsection 5.4.5 Validation of Methods.

The laboratory informs the customer when the method proposed by the customer is considered to be the incorrect choice or the incorrect revision for the intended purpose. This is done as part of contract review addressed in Volume I, Section 4.4 Review of Requests, Tenders and Contracts.

5.4.3 Laboratory Developed Methods

If a laboratory develops methods for its own use, the laboratory has its own procedure for its introduction. This procedure provides the planned activities, identification of qualified personnel, and resources. Plans are revised as method development proceeds and effective communication amongst all personnel involved is strongly encouraged. Laboratory developed methods adopted by the laboratory are used if they are validated according to Volume I, subsection 5.4.5 Validation of Methods.

5.4.4 Non-standard Methods

Non-standard methods are those methods not taken from authoritative, validated sources. A non-standard method has not undergone validation, such as a collaborative study or process to evaluate the method's performance capabilities.

Non-standard methods are selected for use when a customer request cannot be addressed with the use of a standard method. Such methods are subject to agreement with the customer and a clear specification of the customer's work requests, including the purpose of the test, is made. This process is described for contract amendments in Volume I, subsection 4.4.5 Amendments to Contracts with laboratory management concurrence. Non-standard methods are validated according to Volume I, subsection 5.4.5 Validation of Methods.

5.4.5 Validation of Methods

5.4.5.1 Definition

Validation is the confirmation by examination and the provision of objective evidence that the particular specifications for an intended use are fulfilled.

5.4.5.2 Methods Requiring Validation

The laboratory validates non-standard methods, laboratory developed methods, and modified standard methods including use outside the intended scope and applications. Validation is conducted to confirm that the methods are fit for the intended use. The validation is documented.

5.4.5.3 Process

The validation process addresses the needs of the given application or field of application. The laboratory analyst records the results obtained according to the procedure, Volume II, Section 2, ORA-LAB.5.4.5 Methods, Method Verification and Validation. The validation results include a statement as to whether the method is fit for the intended use. The needs of the customer define the intended use of the method. The attributes and data quality objectives include but are not limited to:

- accuracy,
- precision,
- specificity,
- detection limit,
- limit of quantitation,
- linearity,

- range, and
- ruggedness or robustness.

If all the data quality objectives are met as indicated by the data collected, the method is considered as validated.

5.4.6 Estimation of Uncertainty of Measurement

5.4.6.1 Procedure for Calibration Activities

ORA laboratories do not perform calibration activities. At such time that calibration activities are performed, the ORA laboratories are to address the requirements of ISO/IEC 17025, 5.4.6.1.

5.4.6.2 Procedure for Testing Activities

The laboratory has a procedure, Volume II, Section 2, ORA-LAB.5.4.6, Estimation of Uncertainty of Measurement**,** to estimate the uncertainty of measurement for testing activities.

The application of details in cases where the nature of the test method may preclude rigorous, metrologically and statistically valid, calculation of uncertainty of measurement is addressed in the procedure.

An attempt is made to identify all the components of uncertainty and make a reasonable estimation of the measurement uncertainty. This estimation is based on knowledge, experience, and validation data of the performance of the method and on the measurement scope. If needed as a part of the laboratory data, the uncertainty estimation is reported according to the procedure, Volume II, Section 2, ORA-LAB.5.4.6 Estimation of Uncertainty of Measurement.

5.4.6.3 Uncertainty Components

When estimating the uncertainty of measurement, all important uncertainty components are recorded in the uncertainty records for each determination and test technology as addressed in the procedure Volume II, Section 2, ORA-LAB.5.4.6, Estimation of Uncertainty of Measurement.

5.4.7 Control of Data

5.4.7.1 Data Transfers

Calculations and data transfers are reviewed before the data is reported. All changes are identified and verified where they occur. This process is detailed in the procedure for laboratory quality control identified in Volume I, Section 5.9 Assuring the Quality of Test Results**.**

5.4.7.2 Computer Use

When computers or automated equipment are used for the acquisition, processing, recording, reporting, storage or retrieval of test data, the laboratory follows the process in the laboratory's data protection procedure.

5.4.7.2 a. If computer software is developed by the user, its development is documented in detail and algorithms are validated.

5.4.7.2 b. The laboratory's data protection procedure addresses the protection of the data to include, but not limited to data integrity, data confidentiality during entry, collection, storage, transmission and processing.

5.4.7.2 c. Computers and automated equipment are maintained to ensure proper functioning and are provided with the environmental and operating conditions to maintain the integrity of test and data.

Related Procedures

- Volume II, Section 2, ORA-LAB.5.4.5 Validation of Methods
- Volume II, Section 2, ORA-LAB.5.4.6 Estimation of Uncertainty of Measurement
- Each ORA laboratory has its own data protection procedure.

5.5 Equipment

5.5.1 Laboratory Equipment

The laboratory has sample preparation, measurement and test equipment for the correct performance of the tests and calibrations. The laboratory also has ancillary equipment for processing samples and for processing data.

The laboratory purchases the equipment used by the laboratory. Maintenance contracts are established as needed. In those cases where the laboratory leases equipment it has direct control concerning its use. Leased equipment is managed in the same manner as purchased equipment according to the management system requirements.

ORA laboratories maintain an equipment inventory of all laboratory equipment used to perform regulatory testing.

5.5.2 Equipment Capability

Equipment and its software used for testing is to achieve the accuracy expected and comply with specifications of the testing concerned. Laboratory equipment that has a significant effect on the results has a calibration schedule. The equipment performance is verified and verification records are maintained. Equipment is to meet the laboratory's testing parameters and conform to standard specifications before being placed into service.

5.5.3 Authorized Operation

Personnel are authorized to operate equipment according to Volume I, subsection 5.2.5 Management Authorization. Authorization is based on work assignment, training, experience and demonstrated proficiency. Equipment manuals and maintenance procedures are maintained and supplied to laboratory personnel as described in Volume I, subsection 4.3.1 General and Volume II, Section 2, ORA-LAB.5.5.1 Instrument and Equipment Documentation and Records.

5.5.4 Equipment Identification

Each item of equipment used for testing has an FDA property number or an identification number that is unique to each instrument.

5.5.5 Equipment Records

Records are maintained of each item of equipment and its software significant to the tests or calibrations performed according to the procedure in Volume II, Section 2, ORA-LAB.5.5.1 Instrument and Equipment Documentation and Records.

The records include at least the following items:

- identity of the item of equipment and its software;
- manufacturer’s name, type identification, and serial number or other unique identification;

- performance checks that equipment conforms to testing parameters and acceptance criteria;
- location of the equipment;
- manufacturer's instructions;
- dates, results and copies of reports and certificates of calibrations, adjustments, acceptance criteria, and the due date of next calibration;
- maintenance plan and maintenance carried out to date; and
- any damage, malfunction, modification or repair to the equipment.

5.5.6 Management of Equipment

The laboratory has a procedure in Volume II, Section 2, ORA-LAB.5.5 Equipment for the safe handling, transport, storage, use and planned maintenance of measuring equipment to ensure proper functioning and to prevent contamination or deterioration.

5.5.7.1 Out of Service

Equipment that has been subjected to overloading or mishandling, gives suspect results, or has been shown to be defective or outside specified limits, is taken out of service. It is isolated and clearly labeled or marked as being "Out of Service" to prevent its use until it has been repaired and shown by calibration or test to perform correctly.

5.5.7.2 Retesting and Calibration

Laboratory personnel examine the effect of quality control analyses that indicate the defect or departure from specified limits on previous tests according to Volume I, Section 4.9 Control of Non-conforming Work.

5.5.8 Calibration Status

Equipment under the control of the laboratory and requiring calibration is labeled or coded to indicate the calibration status, including the date when last calibrated and the date due for recalibration. Alternatively, equipment calibration status may be identified in an associated record to indicate the status of calibration.

5.5.9 Equipment Leaving the Laboratory

If for any reason equipment leaves the direct control of the laboratory, the function and calibration status of the equipment is checked upon return and shown to be satisfactory before the equipment is returned to service.

5.5.10 Calibration Confirmation

Intermediate calibration confirmation checks are performed to maintain confidence in the calibration status of the equipment. These checks are conducted according to the procedure in Volume I, Section 5.9 Assuring the Quality of Test Results.

5.5.1.1 Correction Factors

Where calibrations give rise to a set of correction factors, these factors are communicated to users.

5.5.12 Safeguards

Test and calibration equipment, including both hardware and software, are safeguarded from adjustments that would invalidate the test or calibration results. Safeguards are provided using access control to the laboratory.

Related Procedures

- Volume II, Section 2, ORA-LAB.5.5 Equipment
- Volume II, Section 2, ORA-LAB.5.5.1 Instrument and Equipment Documentation and Records
- Each ORA laboratory has established equipment maintenance schedules in accordance with the ORA system.

5.6 Measurement Traceability

5.6.1 General

The laboratory equipment is calibrated before being placed into service, as scheduled and following repairs. Procedures for equipment calibration are provided in Volume II, Section 2, ORA-LAB.5.5 Equipment**.**

5.6.2 Specific Requirements

5.6.2.1 Calibration – Requirements for Contracting Metrologists

5.6.2.1.1 Measurement Traceability

The program for calibration of equipment demands that calibrations and measurements made by the laboratory are traceable to the International System of Units. The scheduling of calibration activities is defined in Volume II, Section 2, ORA-LAB.5.5 Equipment, Table 2.

Contracting metrologists providing services to ORA laboratories are to provide evidence of measurement traceability of its own measurement standards and measuring instrument to the SI. This is done by means of an unbroken chain of calibration or comparisons linking them to primary standards of the SI units of measurement. Such primary standards are those used by national measurement standards.

The measurement traceability to SI units may be achieved by measurements related to national measurement standards. National measurement standards may be used as primary standards that are primary realizations of the SI units or agreed representations of SI units. National measurement standards based on fundamental physical constants, or standards calibrated by another national metrological institute may be use as primary standards.

Contracting metrologists providing services to ORA laboratories are to provide documentation demonstrating measurement capability and competence to perform the calibration services requested by ORA laboratories.

Calibration certificates issued by contracting metrologists are to include the measurement results, including the measurement uncertainty and a statement of conformance with an identified metrological specification.

5.6.2.1.2.1 Non-traceability of reference standards to SI units

Calibrations that cannot provide strict measurement traceability to SI units are conducted such that the calibration results can provide confidence in the measurements made in the course of the

analyses. Traceability alternatives to SI units are described in the procedure in Volume II, Section 2, ORA-LAB.5.6 Measurement Traceability.

5.6.2.1.2.2 Interlaboratory comparisons

ORA laboratories participate in FDA's National Check Sample Program, the AOAC Standard Microbiology Proficiency Testing Program, and other national or international proficiency programs, as applicable.

5.6.2.2 Testing

5.6.2.2.1 Testing and calibration activities

The requirements of Volume I, Subsection 5.6.2.1 Calibration-Requirements for Contracting Metrologists are included in the laboratory's calibration program for equipment that has a significant contribution from its calibration to the total measurement uncertainty. Contributions are considered significant if they are greater than a fifth of the largest contributor.

The measurement of uncertainty is determined and recorded according to Volume II, Section 2, ORA-LAB.5.4.6, Estimation of Uncertainty of Measurement.

Equipment that does not contribute appreciably to the total uncertainty of the test result is exempt from the activities described in Volume I, Subsection 5.6.2.1 Calibration-Requirements for Contracting Metrologists.

5.6.2.2.2 Non-traceability to SI Units

Where measurement traceability for testing and calibration activities to SI units is not possible, the policies stated in Volume I, subsection 5.6.2.1 Calibration-Requirements for Contracting Metrologists are followed.

5.6.3 Reference Standards and Reference Materials

5.6.3.1 Reference Standards

The laboratory calibrates its reference standards. Details are included in Volume II, Section 2, ORA-LAB.5.5 Equipment.

A contracting metrologist who is to provide measurement traceability as described in Volume I, subsection 5.6.2.1 calibrates the reference standards.

The reference standards are used for calibration only.

5.6.3.2 Reference Materials

A reference material is a homogenous and well characterized substance used for standardization of equipment used in the testing process. Reference materials are traceable to national or international standard reference materials (SRMs), such as National Institute of Standards and Technology (NIST), or certified reference materials (CRMs) from competent suppliers of reference materials.

The measurement integrity of internal reference materials generated by the laboratory is evaluated against either standard reference materials or certified reference materials from an independent source when it is technically and economically possible.

5.6.3.3 Intermediate Confirmation of Calibration Status

Metrological confirmation for reference standards and reference materials included in the calibration program is conducted according to a schedule addressed in the procedure in Volume II, Section 2, ORA-LAB.5.5 Equipment. The confirmation is conducted to maintain confidence in the calibration status of reference standards and reference materials.

5.6.3.4 Transport and Storage

The procedure found in Volume II, Section, ORA-LAB.5.6 Measurement Traceability**,** addresses the safe handling, transport, storage and use of reference standards and reference materials. These activities are established in order to prevent contamination, deterioration, and to protect the integrity of reference standards and reference materials.

Related Procedures

- Volume II, Section 2, ORA-LAB.5.5 Equipment
- Volume II, Section 2, ORA-LAB.5.6 Measurement Traceability

5.7 Sampling Operations

5.7.1 Procedure

ORA laboratories do not routinely perform sampling in the sense of collecting a representative sample from a product lot to represent the whole.

Sample Collection Conducted by the Customer: Most test samples are obtained and sent to the laboratory by ORA inspectional staff. Instructions for sample collection by such personnel are provided in the Investigations Operations Manual (IOM). Occasionally, laboratory personnel are consulted about sampling parameters such as sample type or size or guidance for a particular sampling or analytical need. The ORA laboratories, however, exert no direct control over such sampling and do not have responsibility for sampling.

Sampling conducted by ORA laboratories involves for the most part those analyses that call for a portion or aliquot of the total sample received by the laboratory to be analyzed. Generally, this calls for mixing or preparing of samples to assure homogeneity before portions are taken for analysis. Sample preparation and subsampling protocols are found in the analytical methods, compliance programs, and assignments.

Related Procedures

- Investigations Operations Manual, Chapter 4 - Sampling

5.8 Handling of Samples

5.8.1 Protection of Samples

The laboratory procedure in Volume II, Section 2, ORA-LAB.5.8 Sample Management, describes the receipt, processing, protection, storage, retention and disposal of samples. This procedure addresses the laboratory activities conducted to protect sample integrity.
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5.8.2 Identification of Samples

The laboratory has a system for uniquely identifying samples. The sample number is used to track its progress from the time the sample is collected in the field until the analysis is completed and the sample is disposed. The sample number is also used to provide traceability between the sample and the data. The numbering system also provides traceability during transfer of samples within the laboratory and between ORA laboratories in the case of administratively transferred samples. The identification system is described in Volume II, Section 2, ORA-LAB.5.8 Sample Management.

5.8.3 Departures, Additions or Exclusions

Upon receipt of the sample, abnormalities or departures from normal or specified conditions, for example contract specifications, analysis requested, and chain of custody, are recorded according to the FACTS Manual and Volume II, Section 2, ORA-LAB.5.8 Sample Management.

When samples received do not meet established acceptance criteria in Volume II, ORA.LAB.5.8 Sample Management, laboratory personnel consult the customer for further instructions before proceeding. Communication with the customer is documented**.**

5.8.4 Protection of Samples During Processing and Storage

The procedure in Volume II, Section 2, ORA-LAB.5.8 Sample Management, provides the details for protecting test items from deterioration, loss or damage during storage and processing. The laboratory has arrangements for storage and security that protect the condition and integrity of samples. Sample security arrangements apply both in the laboratory and in the custodial areas.

5.8.4.1 Processing Instructions

Handling instructions provided with the sample are followed, as well as the instructions in Volume II, Section 2, ORA-LAB.5.8 Sample Management.

5.8.4.2 Monitoring of Environmental Conditions

When samples are held under environmental conditions specified in the test method, those conditions are maintained, monitored and recorded. Monitoring records are collected according to established procedures. These activities are conducted according to the policies stated in Volume I, Section 5.3 Laboratory Environment.

Related Procedures

- Volume II, Section 2, ORA-LAB.5.8 Sample Management
- FACTS Manual
- Each laboratory has a sample storage Work Instruction established in accordance with ORA system.

5.9 Assuring the Quality of Test Results

5.9.1 Quality Control Procedures

The laboratory has quality control procedures to validate the results of tests undertaken according to Volume II, Section 2, ORA-LAB.5.9 Assuring the Quality of Test Results.

The monitoring data is recorded in such a way that trends may be detected, for example, statistical process control charts. Monitoring activities are planned and evaluated according to Volume II, Section 2, ORA-LAB.5.9 Assuring the Quality of Test Results. Monitoring techniques may include, but are not limited to, the following:

a. Scheduled use of certified reference materials and internally generated reference materials;

b. Scheduled participation in interlaboratory comparison or proficiency-testing and calibration programs as described in ORA-DFS.2, National Check Sample Program;

c. Replicate tests using the same or different methods;

d. Retesting of reference materials and retained customer samples; and

e. Correlation of results from tests conducted for different characteristics of a sample.

5.9.2 The laboratory has defined the criteria for quality control data and performs analysis by such means as control charting. When data is found to be outside the established criteria, action is taken in accordance with the laboratory's control of non-conforming work procedure.

Related Procedures

- Volume II, Section 2, ORA-LAB.5.9 Assuring the Quality of Test Results
- ORA.DFS.2, National Check Sample~~s~~ Program
  See at http://intranet.ora.fda.gov/dfs/policies/sops/
- ORA-DFS.1, Microbiological Controls for Sample Analysis
  See at http://intranet.ora.fda.gov/dfs/policies/sops/
- ORA laboratory procedure for handling control of non-conforming work

5.10 Reporting the Results

5.10.1. General

Test reporting is addressed in the procedure found in Volume II, Section 2, ORA-LAB.5.10 Reporting Laboratory Data. This procedure gives the details for reporting data using consistent reporting formats for laboratory worksheets. Reports are reviewed against acceptance criteria that address accuracy, clarity and objectivity. Results are reported on analytical worksheets and in FACTS.

5.10.2 Reporting Results

Data entered onto the worksheets and in FACTS includes all the information specified by ORA as described in the procedure ORA-LAB.5.10 Reporting Laboratory Data of Volume II and the FACTS manual. Other government agency-specified data is recorded by the laboratory on sample forms that accompany the samples.

5.10.3 Additional Requirements for Worksheets

5.10.3.1 Specific Requirements

The following information is included in test reports for the interpretation of the test results:

a. Deviations from, additions to, or exclusions from the test method, and information on test conditions, such as environmental conditions;

b. A statement of conformance or non-conformance with specifications;

c. A statement of the estimated uncertainty of measurement when a customer requests it;

d. Opinions and interpretations as detailed in Volume I, Section 5.10.5; and,

e. Additional information that may be requested by methods, customers or groups of customers.

5.10.3.2 Sampling Results

In addition to the instructions listed in Sections 5.10.2 Reporting Results and 5.10.3.1 Specific Requirements, sampling information and conditions are posted to the laboratory for review on the FACTS sample collection record.

5.10.4 Calibration Certificates

ORA laboratories do not conduct calibration activities and, therefore, do not issue calibration certificates.

5.10.5 Opinions and Interpretations

Laboratory management expresses its opinion and interpretation of the compliance or non-compliance of the results through the laboratory classification assigned to each sample. This laboratory classification is recorded in FACTS and may be recorded on the FDA form FD-465 as well. The laboratory classifications are defined in the FDA Data Codes Manual.

5.10.6 Testing Results Obtained from Subcontractors

Subcontracting laboratories are not utilized by ORA laboratories, therefore, there is no such data found for incorporation in the analysis report to the customer.

5.10.7 Electronic Transmission of Results

In the case of transmission of test or calibration results by telephone, facsimile or other electronic means, such transmission is conducted under conditions that meet the criteria of Volume I, subsection 5.4.7 Control of Data.

5.10.8 Format of Worksheets

The format for laboratory worksheets is designed to accommodate the type of test conducted to minimize the possibility of misunderstanding or misuse. The worksheet format is described in Volume II, Section 2, ORA-LAB.5.10 Reporting Laboratory Data.

5.10.9 Amendments to Worksheet

Material amendments to analytical findings after issue are made only in the form of an additional document. They are flagged “Additional Analyses” in accordance with procedure ORA-LAB.5.10 Reporting Laboratory Data of Volume II. Amendments are to meet the same reporting criteria.

Related Procedures

- Volume II, Section 2, ORA-LAB.5.10 Reporting Laboratory Data
- FDA Regulatory Procedures Manual

Document History

Version 1.2 changes:
Table of Contents – added Document History, page 44
Section 4.2.4, page 10, second bullet item – (technical management) added to Responsible Managers

Issue Date: 01/19/05 By: LMEB

Version 1.3 changes:
Section 4.1, Organization, I. Principal Responsibilities, page 4 - added PHS Act.
Section 4.4.3, page 13 - Volume I Subsection 4.5. title changed from "Subtracting of Tests" to "Subcontracting of Tests".
Section 4.11.2, page 19, first bullet under Related Procedures - added the word "has".
Section 5.2.1, page 25, second paragraph - changed Office of Regional Management to Office of Resource Management.
Section 5.4.2, Selection of Methods, page 29, first paragraph - added after LIBS "that are included in compliance programs and special assignments.
Section 5.4.5.2., page 30 - corrected "amplifications" to "applications".

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Version 1.4 changes:
Quality System and quality system references changed to Management System and management system throughout document.
Table of Contents – page column renumbered
Section 1.0, changed date to 2005.
Section 4.12, add “assignments” to fourth bullet.
Section 4.1.5 a., page 4, added second sentence.
Section 4.1.5 d., page 5, website updated.
Section 4.1.5 k., page 6, added.
Section 4.1.6, page 6, added.
Section 4.2.2 c., page 10, added last sentence.

Section 4.2.3, page 10, added new and moved former 4.2.3. to 4.2.5, page 10.
Section 4.2.4, page 10, added new and moved former 4.2.4 to 4.2.6, page 10.
Section 4.2.7, page 11, added.
Section 4.7, page 17, renumbered with 4.7.1 and added 4.7.2
Section 4.15, Improvement, added to Table of Contents and page 24.
Section 5.2.2.1, page 26, added last sentence to third paragraph.
Section 5.9, page 41, renumbered with 5.9.1 and added 5.9.2; added ORA laboratory procedure for handling control of non-conforming work to Related Procedures.
Section 5.10.9, page 44, revised.

Issue Date: 11/16/05 By: LMEB

Version 1.5 changes:
Table of Contents – Improvement moved to 4.10 & elements moved down; page column renumbered
Section 4.1.5 d., page 5, website updated.
Section 4.2.2, page 7, FDA mission statement deleted & ORA mission statement added; revised second sentence
Section 4.2.2 e., page 10, revised second sentence.
Section 4.3.2, page 12, corrected number to 4.3.3
Section 4.10, page 18, corrected to Improvement to align with ISO 17025:2005
Section 4.11-4.15, pages 19-23, moved elements down one to align with ISO 17025:2005
Section 4.7, page 17, renumbered with 4.7.1 and added 4.7.2

Issue Date: 11/15/07 By: LMEB

Version 1.6 changes:
Section 4.1.5 i. and j, Quality Management System Manager changed to QSM
Section 4.2.6, Quality Manager changed to Quality System Manager
Sections 4.1, 4.11, 4.12, 4.13, 4.14, 4.15, Related Procedures, numbering corrected for procedures
Section 4.8, 4.9.2, 4.11.5, numbering corrected for procedures
Section 5.9 Related Procedues, updated websites

Issue Date: 06/06/08 By: LMEB