

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 1 of 46

Sections in This Document

1. Introduction	2
2. Controlled Distribution of the Quality Manual	2
3. Quality Policy Statement	2
3.1. Management System Objectives	3
3.2. Management System Awareness and Implementation	3
4. General Requirements	3
4.1. Impartiality	3
4.2. Confidentiality	4
5. Structural Requirements	5
5.1. Laboratory as Legal Entity	5
5.2. Management Responsible for Laboratory	5
5.3. Scope of Accredited Laboratory Activities	6
5.4. Laboratory Requirements	6
5.5. Laboratory Organizational Structure and Procedures	6
5.6. Personnel Responsibilities and Authority	7
5.7. Communication and Integrity of the Management System	9
6. Resource Requirements	9
6.1. General	9
6.2. Personnel	10
6.3. Facilities and Environmental Conditions	12
6.4. Equipment	14
6.5. Metrological Traceability	18
6.6. Externally Provided Products and Services	19
7. Process Requirements	21
7.1. Review of Requests, Tenders, and Contracts	21
7.2. Selection, Verification and Validation of Methods	24
7.3. Sampling	27
7.4. Handling of Test or Calibration Items	28
7.5. Technical Records	28
7.6. Evaluation of Measurement Uncertainty	29
7.7. Ensuring the Validity of Results	30

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 2 of 46

7.8. Reporting Results	31
7.9. Complaints.....	34
7.10. Nonconforming Work	35
7.11. Control of Data and Information Management	36
8. Management System Requirements	37
8.1. Options.....	37
8.2. Management System Documentation (Option A).....	37
8.3. Control of Management System Documents (Option A)	40
8.4. Control of Records.....	41
8.5. Actions to Address Risks and Opportunities.....	41
8.6. Improvement.....	42
8.7. Corrective Actions	42
8.8. Internal Audits	43
8.9. Management Reviews.....	44
9. Document History	45
10. Change History	45
11. Attachments.....	46

1. 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 17025:2017).

2. Controlled Distribution of the Quality Manual

The Office of Regulatory Science (ORS) is responsible for maintaining the official master copy of the ORA Laboratory Manual which contains the ORA Laboratory Quality Manual. This Manual consists of Volume I, ORA Laboratory Manual of Management Requirements and Volume II, ISO 17025:2017 ORS Laboratory Procedures. The ORA Laboratory Manual also includes operational procedures and training in Vol III and Vol IV respectively. General distribution of this manual is accomplished using a computer network. Biennial review is coordinated by the Office of Regulatory Science.

3. Quality Policy Statement

ORA's mission statement states "ORA protects consumers and enhances public health by maximizing compliance of FDA regulated products and minimizing risk associated

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 3 of 46</p>

with those products”. ORS laboratories are committed to providing testing that meets both the needs of the customers and the requirements of ISO/IEC 17025:2017 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.

3.1. Management System Objectives

3.1.1. The primary objective of the management system established by ORS 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:

- A. accuracy,
- B. precision,
- C. detection and quantitation limits,
- D. timeliness, and
- E. comparability.

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

3.1.3. Third, strive to meet or exceed the customer’s needs and expectations.

3.1.4. Fourth, maintain ORS laboratories’ reputation for quality by fostering continuous process improvement and problem prevention.

These objectives are considered as part of the reviews performed by management.

3.2. 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 ORA Laboratory Manual, Volume II, ORA-LAB.5.2 Personnel Training and Competency Management.

4. General Requirements

4.1. Impartiality

4.1.1. To avoid conflicts of interest, pressures, and influences, FDA employees

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 4 of 46</p>

are familiar with and observe the Standards of Ethical Conduct. These principles of ethics can be found at the FDA Division of Ethics and Integrity intranet site.

- 4.1.2. Laboratory management is committed to sustaining impartiality of all personnel by enforcing existing FDA policies and requirements on ethics that were implemented to ensure impartiality in the agency's work.

The FDA provides several means to ensure impartiality of its employees, such as the HHS 520 Request for Approval of Outside Activity and OGE 450 Confidential Financial Disclosure Report Filer forms which are filled out annually and reviewed by the FDA Division of Ethics and Integrity to identify potential risks in relationships, ownership, finances, contracts, etc. that may impact personnel's neutrality regarding FDA related activities. In addition, a monthly list of significantly regulated organizations is distributed for review in keeping with 18 USC § 208 prohibiting personal and substantial participation in matters that have direct and predictable effect on their financial interests.

The Office of Government Ethics (OGE) also requires one hour of ethics training annually. Training is provided on ethics rules, regulations, and integrity 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 6.2.

- 4.1.3. Risks to impartiality are continuously reviewed and eliminated or minimized to ensure there is no compromise to the objectivity of staff engaged in laboratory activities. Employees are familiar with and observe the Standards of Ethical Conduct. 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.
- 4.1.4. Risks to impartiality may be identified during required routine disclosures by employees, management reviews, or during audits. When laboratory employees or processes pose a risk to impartiality, an assessment is made of the nature of the risk and appropriate corrective actions are taken by the laboratory and/or the designated agency authority.

4.2. Confidentiality

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 5 of 46</p>

- 4.2.1. All FDA staff certify their agreement to abide with 5 USC § 552a(1) the Privacy Act and 21 USC § 331 The Trade Secret Act when completing Computer Security Awareness training. Contract employees are required to sign FDA FORM 3398 Commitment to Protect Non-Public Information Employee Agreement upon entry to duty. This form certifies their agreement to abide with 21 U.S.C. 331(j), 21 U.S.C 360j(c), and 18 U.S.C 1905. Confidentiality requirements are included in purchasing agreements, as needed, with vendors performing work in areas where laboratory work is performed.
- 4.2.2. ORS laboratories do not release confidential information to external parties. ORA's Office of Strategic Planning and Operational Planning, Division of Information Management Disclosure Policy manages ORA's information disclosure functions.
- 4.2.3. Reports of information and data are transmitted and filed in accordance with official policies, directives, and notices of the department and the agency. Most reports are only transmitted internally within the agency, 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.
- 4.2.4. FDA facilities are controlled-access buildings to further ensure protection of data. Names and purpose of all non-FDA visitors are provided to security prior to planned visits. Additional department policies are in place for visitors from other countries. Visitors are continuously escorted by FDA representatives and allowed only in areas approved by mandated security protocols in place to ensure no customer or federal information is compromised. Additionally, employees sign commitments to properly keep and use confidential information obtained or witnessed during their duties.

5. Structural Requirements

5.1. Laboratory as Legal Entity

The Food and Drug Administration (FDA) is a government agency under the Department of Health and Human Services (DHHS). 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.) ORS laboratories are legally responsible for all activities within their operations.

5.2. Management Responsible for Laboratory

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 6 of 46</p>

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

The Director of the Office of Regulatory Science is responsible for issuing policy and procedures for the ORS laboratories and monitoring their implementation.

Laboratory management, analysts, and quality managers are 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.

5.3. Scope of Accredited Laboratory Activities

Laboratory activities encompass all processes from the review of vendors for external products and services to sample, equipment, supply, and data handling and reporting within the laboratory. All ORS laboratories have documented training, proficiency, and method validation and verification programs in place. To ensure consistency in these processes controlled, approved documents are maintained to provide guidance in all processes and records retained to recreate processes, if needed. These also provide the basis to evaluate risks and improvements where gaps are identified through nonconformances, complaints, and annual management review of the inputs and outputs of operations.

5.4. Laboratory Requirements

5.4.1. The intent of ORA is to operate testing laboratories per the following requirements:

- A. FDA policies and procedures,
- B. ISO/IEC 17025:2017,
- C. Customer contracts (workplan),
- D. ORA compliance programs and assignments,
- E. Federal and State laws and regulations, and
- F. Accreditation registrar requirements.

5.4.2. ORS laboratories operate permanent facilities across the United States and Puerto Rico at the locations identified in the Staff Manual Guides (SMG), 1121.92 Office of Medical Products and Specialty Laboratory Operations and 1121.93 Office of Food and Feed Laboratory Operations.

5.5. Laboratory Organizational Structure and Procedures

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 7 of 46</p>

5.5.1. The regulatory laboratories are a part of the Office of Regulatory Affairs, FDA and are identified in SMG 1121.9 series. The organization and the relationship among the laboratory staff is reflected in the laboratory’s organizational chart maintained by the laboratory. These charts provide relationships between management, technical operations, and support personnel.

5.5.2. 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 on the U.S. Office of Personnel Management website.

Job responsibilities for laboratory employees are documented in the management system procedures and operating instructions. Position descriptions are maintained by the Office of Talent Solutions (OTS).

- 5.5.3. The laboratory management system is outlined in the following documents:
- A. Quality manual,
 - B. Written procedures,
 - C. Work Instructions,
 - D. References, and
 - E. Forms and records.

This management system is established to address the requirements in ISO/IEC 17025:2017. Each entity establishes and maintains documents per the procedure for document control. The quality policy and quality objectives for ORS laboratories are included in Volume 1, section 3. The documents listed above are accessible to all personnel and are included in the laboratory’s training program.

5.6. Personnel Responsibilities and Authority

Laboratory personnel are aware of their roles and contributions in the management system and of its objectives through regularly scheduled training provided by the quality staff. Laboratory personnel irrespective of other responsibilities have the authority and resources to carry out their duties.

- 5.6.1. General roles and responsibilities for ORS laboratory personnel are summarized as follows:
- A. Quality System Manager

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 8 of 46</p>

1. Ensures that the management system is established, implemented, and maintained in conformance with the requirements of ISO/IEC 17025:2017.
 2. Advocates and coordinates quality improvements to the management system.
- B. Responsible Managers (technical management)
1. Oversee technical functions.
 2. Ensure compliance with the requirements of ISO/IEC 17025:2017.
 3. Ensure management system procedures, applicable standards, specifications, and regulations are followed.
 4. Ensure that qualified, skilled, and trained personnel and other resources are available.
 5. Ensure that products and services satisfy customer requirements.
- C. Analysts and support staff
1. Ensure the quality of their work.
 2. Operate in conformance with the requirements of the management system.
- 5.6.2. All laboratory employees have the authority and are encouraged to identify and report deviations from the management system or procedures for laboratory activities.
- 5.6.3. All laboratory employees contribute toward initiation of actions to minimize such deviations or provide input toward improvement to the system. These actions are monitored and reviewed by laboratory management.
- 5.6.4. The laboratory Quality System Manager (QSM) is responsible for monitoring the laboratory's management system and reporting its performance and any need for improvement to laboratory management.

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 9 of 46</p>

- 5.6.5. Laboratory Management is responsible for the technical operations of the laboratory. Resources for training, laboratory methods, measurement traceability, and purchasing are described in other sections of this Volume and in relevant FDA procedures and policies.
- 5.6.6. Qualified laboratory personnel are assigned to serve in the absence of key managerial personnel, such as Laboratory Director, Quality System Manager, and Supervisors to maintain unbroken continuation of operations. In addition the laboratory has an active and executable contingency plan for the Continuity of Operations (COOP) in place with effectiveness drills enacted at least once each year.

5.7. Communication and Integrity of the Management System

- 5.7.1. Effective communication from management occurs through, but is not limited to, memos, newsletters, electronic presentations, emails, or verbally to laboratory personnel regarding the effectiveness of the management system and the importance of meeting customer, statutory, and regulatory requirements
- 5.7.2. 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 in a policy or procedure are made.

6. Resource Requirements

6.1. General

Personnel, facilities, equipment, systems, and support services necessary for the management and performance of laboratory activities are evaluated and put in place to ensure defensible data and conformity to the requirements of ISO/IEC 17025:2017 General requirements for the competence of testing and calibration laboratories.

- 6.1.1. The sections following below address the factors affecting the correctness and reliability of the tests performed by a laboratory. These factors include contributions from:
 - A. Personnel (MAN-000035 ORA Laboratory Manual, Volume II, ORA-LAB.5.2 Personnel Training and Competency Management),
 - B. Facilities and environmental conditions (MAN-000036 ORA Laboratory Manual, Volume II, ORA-LAB.5.3 Facilities and Environmental Conditions),

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 10 of 46</p>

- C. Equipment (MAN-000039 ORA Laboratory Manual, Volume II, ORA-LAB.5.5 Equipment),
- D. Metrological traceability (MAN-000037 ORA Laboratory Manual, Volume II, ORA-LAB.5.4.5 Methods, Method Verification and Validation; MAN-000041 ORA-LAB.5.6 Measurement Traceability), and
- E. Externally provided products and services (MAN-000027 ORA Laboratory Manual, Volume II, ORA-LAB.4.6 Purchasing and Receipt)

6.1.2. The procedures listed in each section address these factors.

6.2. Personnel

6.2.1. Personnel

All laboratory personnel that could influence laboratory activities act impartially, are competent, and perform their work according to the laboratory's management system. These positions include, but are not limited to analysts, supervisors and managers, laboratory support staff, sample custodians, and administrative management staff.

6.2.2. Competence Requirements

- A. Competence is based on education, experience, demonstrated skills, and training. Staff records contain the documentation of personnel education, qualification, experience, technical knowledge, skills, and training for the position held.
- B. Skills of personnel are based upon demonstration of competence. Competency requirements for each function influencing the results of laboratory activities are documented in the laboratory's training documents. This demonstration is to be completed successfully before laboratory personnel 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.

6.2.3. Personnel Competence

- A. Laboratory management ensures that laboratory personnel have the competence to perform their duties and to evaluate the significance of deviations.
- B. Trainees undergo a training program in accordance with the laboratory's training documents and ORA Office of Training, Education and Development (OTED) standards. Trainees perform procedures when training and competency has been demonstrated. The documented

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 11 of 46</p>

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.

6.2.4. **Communication of Duties, Responsibilities and Authorities**

- A. Job duties, responsibilities and authorities for laboratory employees are documented in the management system procedures and operating instructions.
- B. Position descriptions are maintained by the Office of Talent Solutions (OTS). The laboratory maintains active job descriptions for managerial, technical, and key support personnel involved in laboratory activities. Job descriptions are established based on current duties and technologies utilized.
- C. The laboratory employees involved in laboratory activities have access to consensus standards, instrument manufacturers' manuals, and laboratory procedures for reference.
- D. Effective communication from management occurs through, but not limited to, memos, newsletters, electronic presentations, emails, or verbally to laboratory personnel regarding the effectiveness of the management system.

6.2.5. **Personnel Procedures**

- A. The procedure for determining competence requirements are defined in the laboratory's documents and MAN-000035 ORA-LAB.5.2 Personnel Training and Competency Management.
- B. The Food and Drug Administration's, Office of Talent Solutions (OTS) establishes the hiring procedures for the agency.
- C. 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 can 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.
- D. Training needs are identified in accordance with the analyst's discipline (e.g., Chemist, Microbiologist) and FDA ORA/OTED standards. In-house training is conducted per laboratory's training procedure. Present and anticipated tasks of the laboratory are addressed in the planning of special training modules.

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 12 of 46

E. 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.

F. 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.

Supervisors are designated, and trainees do not perform regulatory work until competent as per the laboratory training program.

G. Personnel are authorized to perform specific laboratory activities according to section 6.2.6 and local documents.

H. Personnel competency is monitored through onsite reviews, reporting and worksheet write-ups, demonstration through documentation of the required instrument maintenance and function checks, results obtained on proficiency test samples, number of samples analyzed satisfactorily and QC samples within established criteria.

6.2.6. Personnel Authorization

A. The Laboratory Management authorizes personnel to perform specific laboratory activities, including but not limited to:

1. Development, modification, verification, and validation of methods.
2. Analysis of results, including statements of conformity or opinions and interpretations.
3. Report, review, and authorization of results.

B. 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/References

- MAN-000035 ORA Laboratory Manual, Volume II, ORA-LAB.5.2 Personnel Training and Competency Management

6.3. Facilities and Environmental Conditions

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 13 of 46

6.3.1. **Suitability of Facilities and Environmental Conditions**

The laboratory environmental conditions facilitate the correct performance of analytical testing. 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.

6.3.2. **Documentation of Requirements for Facilities and Environmental Conditions**

Test methods and environmental monitoring procedures used by the laboratory include instructions addressing applicable environmental conditions.

6.3.3. **Monitoring, Controlling and Recording Environmental Conditions**

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

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

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

C. 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.

6.3.4. **Measures to Control Facilities**

The following measures to control facilities are implemented, monitored and periodically reviewed:

A. Access and use of areas affecting laboratory activities

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 14 of 46</p>

ORS laboratories are limited access areas. Access and use is controlled by, but is not limited to:

1. issuance of keycards for entrance,
2. escorting visitors,
3. issuance of identification badges, and
4. the use of security guards.

B. Housekeeping

Laboratory areas are maintained clean and orderly to prevent contamination of samples and to facilitate the efficiency of laboratory operations. MAN-000036 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.

C. Cross-contamination

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

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

Related Procedures/References

- MAN-000036 ORA Laboratory Manual, Volume II, ORA.LAB.5.3, Facilities and Environmental Conditions.
- Laboratory Chemical Hygiene Plan.
- Laboratory Waste Management Plan.

6.3.5. Work Performed Outside the Laboratory's Permanent Control

In the event staff perform laboratory activities at sites outside of the laboratory's control, facility and environmental requirements are met.

6.4. Equipment

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 15 of 46</p>

6.4.1. Access to Laboratory Equipment

- A. 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. Also see section 6.5 Metrological Traceability.
- B. The laboratory or other ORA component, i.e., Office of Regulatory Science, 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.
- C. ORS laboratories maintain an equipment inventory of all laboratory equipment used to perform regulatory testing.

6.4.2. Equipment Outside the Laboratory's Permanent Control

If for any reason equipment leaves the direct control of the laboratory the laboratory ensures the equipment requirements are met before using the equipment.

6.4.3. Procedure for Handling, Transport, Storage, Use and Planned Maintenance of Equipment

The laboratory has procedures in MAN-000039 Volume II, Section 2, ORA-LAB.5.5 Equipment and MAN-000041 ORA-LAB.5.6 Measurement Traceability for the safe handling, transport, storage, use and planned maintenance of equipment to ensure proper functioning and to prevent contamination or deterioration.

6.4.4. Verification of Equipment Prior to Being Placed or Returned into Service

- A. 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 or returned into service.
- B. Procedures for equipment verification are provided in MAN-000039 Volume II, Section 2, ORA-LAB.5.5 Equipment.

6.4.5. Equipment Accuracy/Uncertainty

Equipment and its software used for testing are to achieve the accuracy expected, measurement uncertainty required, and comply with specifications of the testing concerned.

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 16 of 46

The uncertainty contributions are addressed in MAN-000038 ORA Laboratory Manual, Volume II, Section 2, ORA-LAB.5.4.6. Estimation of Uncertainty of Measurement.

6.4.6. Equipment Calibration

Measuring equipment is calibrated when the measurement accuracy or uncertainty affect the reported results and/or calibration of the equipment is required to establish metrological traceability of the reported result.

Procedures for equipment calibration are provided in MAN-000039 Volume II, Section 2, ORA-LAB.5.5 Equipment and MAN-000041 ORA-LAB.5.6 Measurement Traceability.

6.4.7. Calibration Program

The equipment calibration program is defined in MAN-000039 Volume II, Section 2, ORA-LAB.5.5 Equipment and MAN-000041 ORA-LAB.5.6 Measurement Traceability. These procedures are reviewed and revised according to MAN-000026 ORA-LAB.4.3 Document Control and Management.

6.4.8. Calibration Status

Equipment under the control of the laboratory and requiring calibration, or having a defined period of validity, is labeled or coded to indicate the calibration status or period of validity. Alternatively, equipment calibration status may be identified in an associated record to indicate the status of calibration.

6.4.9. 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 to prevent its use or 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.

Laboratory personnel examine the effect of the defect or departure from specified limits on previous tests according to Volume I, Section 7.10 Non-conforming Work.

6.4.10. 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 7.7 Ensuring the Quality of Test Results.

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 17 of 46</p>

Metrological confirmation for reference standards and reference materials included in the calibration program is conducted according to a schedule addressed in the procedure in MAN-000039 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.

6.4.11. Correction Factors

Where calibrations give rise to a set of correction factors, these factors are updated and implemented to meet specified requirements.

6.4.12. 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.

6.4.13. Equipment Records

Records are maintained of each item of equipment and its software that can influence laboratory activities according to the procedure in MAN-000040 Volume II, Section 2, ORA-LAB.5.5.1 Instrument and Equipment Documentation and Records.

The records include at least the following items, where applicable:

- A. identity of equipment, including its software and firmware version.
- B. manufacturer's name, type identification, and serial number or other unique identification.
- C. evidence of verification that equipment conforms with specified requirements.
- D. current location of the equipment.
- E. calibration dates, results and copies of reports and certificates of calibrations, adjustments, acceptance criteria, and the due date of next calibration or the calibration interval.
- F. documentation of references materials, results, acceptance criteria, relevant dates and the period of validity.
- G. maintenance plan and maintenance carried out to date, where relevant to the performance of the equipment; and
- H. details of any damage, malfunction, modification, or repair to the equipment.

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 18 of 46</p>

6.5. Metrological Traceability

6.5.1. Establishing and maintaining metrological traceability

The program for calibration of equipment demands that calibrations and measurements made by the laboratory are traceable to the International System of Units.

Calibration laboratories providing services to ORS 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.

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

6.5.2. Ensuring measurement results are traceable

- A. Calibration laboratories providing services to ORS laboratories are to provide documentation demonstrating measurement capability and competence to perform the calibration services requested by ORS laboratories.
- B. 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.
- C. 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.

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 19 of 46</p>

6.5.3. 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 MAN-000041 Volume II, Section 2, ORA-LAB.5.6 Measurement Traceability.

6.6. Externally Provided Products and Services

6.6.1. Suitability of Externally Provided Products and Services

The laboratory ensures that only suitable externally provided products and services that affect laboratory activities are used when they are intended for incorporation into the laboratory's activities and/or used to support the operation of the laboratory.

ORS laboratories do not subcontract routine analyses within their 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.

Subcontracting Laboratories

Based on workload fluctuations and resource needs, ORS 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 per Department of Transportation (DOT), United States Post Office (USPS), and carrier regulations. ORA Laboratory Manual (LM), Volume III, Section 2, Chain of Custody describes the procedure for documenting administratively transferred samples (ATS).

Notification of Customer

FACTS (Field Accomplishment and Compliance Tracking System), which is accessible to the customer, serves as a notice of the transfer.

Laboratory Responsibility

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

Related Procedures/References

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 20 of 46</p>

- MAN-000046 ORA Laboratory Manual, Volume III, Section 2, Chain of Custody – Sample Handling

6.6.2. **Purchasing services and supplies**

- A. MAN-000027 ORA-LAB.4.6 Purchasing and Receipt provides policies and instructions for procurement of supplies, materials, equipment, and services that affect the quality of tests. It documents the procedures for purchase, reception, and storage of supplies, materials, and equipment relevant to tests.
- B. 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.
- C. 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.

Records of supplier evaluations are maintained by purchasers of laboratories equipment, services, and supplies.

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. Inspection or verification criteria are used to establish conformance with requests made by the customer, included in standard specifications, or defined in the methods.

- D. Records of unsatisfactory materials and supplies and their disposition are maintained. These records establish trends in vendor performance and ensure that continuing quality material is accepted. A vendor is considered unacceptable and is not used when the quality of product or service does not meet expectations or specifications.

6.6.3. **Communicating requirements to external providers**

Critical specifications and requirements are clearly described on the purchasing requests and are communicated to external providers by the Purchasing Agent. These criteria include:

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 21 of 46</p>

- A. The products and services to be provided.
- B. The acceptance criteria; and
- C. Competence, including any required qualification of personnel

ORS laboratories do not subcontract routine analyses within their scope of accreditation.

Related Procedures/References

- 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

7. Process Requirements

7.1. Review of Requests, Tenders, and Contracts

7.1.1. Procedure

ORA, Division of Planning and Evaluation (DPE) develops and issues the Annual Fiscal Year (FY) Workplan for ORA field units. The portion of the workplan concerned with the ORS laboratories is a cooperative effort among the Centers, ORA Field Committee, and ORS. The workplan is based on several factors such as the budget, the number of analysts and number 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 ORS laboratories and ORS 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 GUID-000250 A Guide to Understanding the Program-based Forecast for Work planning or through consultation with ORS management.

In addition to the workplan, assignments may be issued to ORS laboratories by an ORA headquarters unit or a Center. Multiple program assignments and high priority requests for work are approved per FDA Field Management

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 22 of 46</p>

Directive 17, ORA Field Assignments-Guidelines for Issuance by Headquarters. Such assignments are cleared through the Office of Strategic Planning and Operational Policy (OSPOP). 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.

7.1.2. Subcontracting Laboratories

The policies regarding the use of subcontracting laboratories are found in Volume I Subsection 6.6 Externally Provided Products and Services. 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.

Based on workload fluctuations and resource needs, ORS 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.

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

Laboratory methods are selected based on compliance programs. 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 7.2.2 Validation of Methods.

7.1.3. Method Requested is Inappropriate or Out of Date

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 section 7.1.1.

7.1.4. Statements of Conformity

When the customer requests a statement of conformity to a specification or standard for the test, the specification or standard and the decision rule are clearly defined in the compliance programs or standard. Otherwise, the laboratory communicates the decision rule selected to the customer and

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 23 of 46</p>

obtains their agreement. See section 7.8.6 Reporting Statements of Conformity.

7.1.5. Differences and Deviations

The ORS laboratories and ORS 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 prior to commencing work and in accordance with GUID-000250 A Guide to Understanding the Program-based Forecast for Work planning, or through consultation with ORS management.

7.1.6. Communicating with the customer

Requests for deviations from work assignments or compliance programs are processed by the Office of Regulatory Science (ORS). ORS interacts with the customer to determine whether the requested changes are acceptable and do not impact the integrity of the laboratory or the validity of the results. Records of contract changes are maintained.

7.1.7. 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.

7.1.8. Customer Service

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 7.1.1. The laboratory maintains communications regarding deviations from contract work. Communications regarding compliance programs, workplan and assignments are conducted through ORS.

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

7.1.9. Records of Review

ORS laboratories maintain records of workplan reviews, changes, and change requests. Records are also maintained of discussions regarding ad hoc assignments.

Related Procedures/References

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 24 of 46</p>

- GUID-000250 A Guide to Understanding the Program-based Forecast for Work planning
- FDA Field Management Directive 17, ORA Field Assignments-Guidelines for Issuance by Headquarters
- Annual Workplan

7.2. Selection, Verification and Validation of Methods

7.2.1. Selection and Verification of Methods

Specific requirements for the Verification and Validation of methods process for ORS laboratories are outlined in MAN-000037 ORA-LAB.5.4.5 Method Validation and Verification.

- A. The scope of test technologies and associated method source routinely used are identified in the laboratory's accreditation program documentation.
- B. The estimation of the uncertainty of measurement is addressed in Volume I, subsection 7.6. Volume I, Section 7.7 Ensuring the Validity of Results of this manual describes the quality control processes, including the application of statistical techniques, for supporting test and calibration data.
- C. Laboratory methods and supporting documents are controlled according to Volume I, Section 8.3 Control of Management System Documents and are readily available.
- D. Laboratory methods are selected to meet the customer's need as addressed in Volume I, Section 7.1 Review of Requests, Tenders and Contracts. The laboratory ensures that it uses the latest valid version of analytical methods unless not appropriate or possible to do so.
- E. 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 AOAC INTERNATIONAL or any supplement of any of them, American Public Health Association

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 25 of 46

(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 Macro analytical 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. Standard methods are verified according to the procedure, MAN-000037 Volume II, Section 2, ORA-LAB.5.4.5 Methods, Method Verification and Validation.

F. 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 7.2.2 Validation of Methods.

G. The laboratory informs the customer when the method proposed by the customer is an incorrect choice or the incorrect revision for the intended purpose. This is done as part of contract review addressed in Volume I, Section 7.1 Review of Requests, Tenders and Contracts.

7.2.2. Standard methods are verified according to the procedure, MAN-000037 Volume II, Section 2, ORA-LAB.5.4.5 Methods, Method Verification and Validation.

Records of the verification are retained by the ORS laboratories. If the method is revised by the issuing body, verifications are repeated to the extent necessary.

7.2.3. Non-standard methods are those methods not taken from authoritative, validated sources. A nonstandard 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

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 26 of 46</p>

process is described for contract amendments in Volume I, subsection 7.1 Amendments to Contracts with laboratory management concurrence. Non-standard methods are validated according to Volume I, subsection 7.2.2 Validation of Methods.

7.2.4. When a laboratory develops methods for its own use refer to MAN-000037 Volume II, Section 2, ORA-LAB.5.4.5. This procedure provides the planned activities, identification of competent personnel, and resources. Method development plans are reviewed periodically to confirm the customer's requirements are still being met. Any modifications to the development plan shall be approved and authorized. Laboratory developed methods adopted by the laboratory are used if they are validated according to Volume I, subsection 7.2.2 Validation of Methods.

7.2.5. Deviations from test methods are documented, technically justified, authorized, and where circumstances call for it, accepted by the customer according to MAN-000044 Volume II, Section 2, ORA-LAB.5.10 Reporting Laboratory Data.

7.2.6. Validation of Methods

- A. The laboratory validates non-standard methods, laboratory developed methods, and modified standard methods including use outside the intended scope or otherwise modified. Validation is conducted to confirm that the methods are fit for the intended use, relevant to the customers' needs, and consistent with specified requirements. The validation is as extensive as is necessary to meet the needs of the given application or field of application.
- B. When changes are made to a validated method, the influence of such changes shall be determined and where they are found to affect the original validation, a new method validation shall be performed.
- C. 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, MAN-000037 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:

- 1. accuracy,

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 27 of 46

2. precision,
 3. specificity,
 4. detection limit,
 5. limit of quantitation,
 6. linearity,
 7. range, and
 8. ruggedness or robustness.
- D. If all the data quality objectives are met as indicated by the data collected, the method is considered as validated.
- E. The following records are maintained for each validation:
1. the validation procedure used.
 2. specification of the requirements
 3. determination of the performance characteristics of the method.
 4. results obtained.
 5. a statement on the validity of the method, detailing its fitness for the intended use.

7.3. Sampling

- A. ORS laboratories do not routinely perform sampling in the sense of collecting a representative sample from a product lot to represent the whole.
- B. Sample Collection Conducted by the Customer: Most test samples are obtained and sent to the laboratory by ORA inspectional staff. Instructions for sample collection, including methods and sampling plans, by such personnel are provided in the Investigations Operations Manual (IOM) Chapter 4.
- C. Occasionally, laboratory personnel are consulted about sampling parameters such as sample type or size or guidance for a sampling or analytical need. The ORS laboratories, however, exert no direct control over such sampling and do not have responsibility for sampling.
- D. Sampling data (i.e., date and time of sampling, description, environmental conditions, collector identification, etc.) required as part of testing is included in the Collection Report accompanying the request in FACTS. When the request is entered, a unique identifier is assigned to the sample.
- E. Sampling conducted by ORS laboratories involves for the most part those analyses that call for a portion or aliquot of the total sample received by the

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 28 of 46</p>

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.

7.4. Handling of Test or Calibration Items

The laboratory procedure in MAN-000042 Volume II, Section 2, ORA-LAB.5.8 Sample Management, describes the receipt, processing, protection, storage, retention, and disposal of samples. This procedure also provides the details for handling and 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.

7.4.1. 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 ORS laboratories in the case of administratively transferred samples. The identification system is described in MAN-000042 Volume II, Section 2, ORA-LAB.5.8 Sample Management.

7.4.2. When samples received do not meet established acceptance criteria, for example, contract/program specifications, analysis requested, abnormalities or departures from normal or specified conditions, and chain of custody criteria, these deviations are recorded according to MAN-000042 Volume II, Section 2, ORA-LAB.5.8 Sample Management. The customer is consulted prior to commencement of analysis for further instructions. Communication with the customer is recorded in accordance with SOP-000285 Sample Feedback Report Process.

Sample abnormalities or departures are also noted on the analytical worksheet.

7.4.3. When samples and calibration items have specific environmental conditions, 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 Section 6.3 Facilities and Environmental Conditions.

7.5. Technical Records

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 29 of 46</p>

- 7.5.1. Technical records for all activities that contribute to data reporting, depending on the type of analysis, include the original observations, derived data, calculations, standard preparation, instrument printouts, and results. These records contain the date each activity is completed and the identity of all persons who perform each activity throughout the process, including those who review the data and results.
- 7.5.2. Observations, data, and calculations are recorded at the time they are made and are identifiable to the activity performed.
- 7.5.3. The records of each test contain sufficient information to repeat the test under conditions as close as possible to the original. This information includes environmental conditions that affect the test and factors that affect the measurement results and its associated measurement uncertainty.
- 7.5.4. Staff records, equipment calibration, and verification reports are retained in accordance with the laboratory's control of records procedure. These records contain sufficient information to establish an audit trail. The requirements for an audit trail in laboratory records are outlined in MAN-000032 ORA-LAB.4.13 Record and Data Management.
- 7.5.5. Data is reported electronically in FACTS and/or scanned and uploaded into Compliance Management Services (CMS), both ORA web-based programs.
- 7.5.6. 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.
- 7.5.7. ORS laboratories ensure changes to technical records can be tracked to the previous version or to original observations. Both the original and amended data and files are retained, including the date the record was changed, an indication of what was changed and the person responsible for the alteration.

7.6. Evaluation of Measurement Uncertainty

7.6.1. 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 MAN-000038 Volume II, Section 2, ORA-LAB.5.4.6, Estimation of Uncertainty of Measurement.

7.6.2. Procedure for Calibration Activities

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 30 of 46</p>

ORS laboratories do not perform calibration activities. At such time that calibration activities are performed, the ORS laboratories are to address the requirements of ISO/IEC 17025:2017.

7.6.3. Procedure for Testing Activities

The laboratory has a procedure, MAN-000038 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, MAN-000038 Volume II, Section 2, ORA-LAB.5.4.6 Estimation of Uncertainty of Measurement.

7.7. Ensuring the Validity of Results

7.7.1. Quality Control Procedures

The laboratory has quality control procedures to validate the results of tests undertaken according to MAN-000043 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 MAN-000043 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 or quality control materials.
- B. Use of alternative instrumentation that has been calibrated to provide traceable results.
- C. Functional check(s) of measuring and testing equipment.
- D. Use of check or working standards with control charts.
- E. Intermediate checks on measuring equipment.
- F. Replicate tests using the same or different methods.

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 31 of 46

- G. Retesting of reference materials and retained customer samples.
 - H. Correlation of results from tests conducted for different characteristics of a sample.
 - I. Review of reported results.
 - J. Scheduled participation in interlaboratory comparison or proficiency-testing and calibration programs as described in SOP-000935 National Check Sample Program.
 - K. Testing of blind samples.
- 7.7.2. ORS laboratories participate in proficiency testing programs and/or interlaboratory comparisons other than proficiency testing, where available and appropriate.
- 7.7.3. 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 MAN-000029 ORA-LAB.4.9 Control of Nonconforming Work.

7.8. Reporting Results

7.8.1. General Requirements

Test reporting is addressed in the ORA Laboratory Manual procedure found in MAN-000044 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. Results are reported on analytical worksheets and in FACTS and/or LIMS.

- A. Laboratory results are reviewed and authorized for release by supervisors or designees. Reports are reviewed for accuracy, clarity and objectivity. 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/or LIMS and may be recorded on the FDA form FD-465 as well. The laboratory classifications are defined in the ORA Laboratory Manual Vol. III, Section 3.
- B. 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/or LIMS and final review is performed. An electronic test

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 32 of 46</p>

report is in FACTS and/or LIMS. Staff records, equipment calibration, and verification reports are retained in accordance with the laboratory's control of records procedure.

- C. The records contain sufficient information to establish an audit trail.
- D. 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.
- E. 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.
- F. Test reporting is addressed in the procedure found in MAN-000044 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.

7.8.2. **Common Requirements for Reports (test, calibration, or sampling)**

A. Format

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 MAN-000044 Volume II, Section 2, ORA-LAB.5.10 Reporting Laboratory Data.

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

B. Data Provided by Customer

Analysts describe the sample as received, including any information provided by the customer, on the sample worksheet in the description of sample block (Block 7). Unless noted in the sample worksheet, results apply to the sample as received.

7.8.3. **Specific Requirements for Test Reports**

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

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 33 of 46</p>

1. Information on test conditions, such as environmental conditions.
2. Where relevant, a statement of conformance or non-conformance with specifications.
3. The measurement uncertainty presented in the same unit as the measurand, or in a term relative to the measurand when:
4. It is relevant to the validity of the test results.
5. A customer requires it, or;
6. The measurement uncertainty affects conformity to a specification limit.
7. Opinions and interpretations as detailed in Volume I, Section 7.8.7; and,
8. Additional information that may be requested by methods, customers, or groups of customers.

7.8.4. Specific Requirements for Calibration Certificates

ORS laboratories conduct in-house calibration activities on measuring and test equipment only and, therefore, do not issue calibration certificates. In-house calibrations are documented by a report, or sticker, or other suitable method.

7.8.5. Reporting Sampling – specific requirements

In addition to the instructions listed in Sections 7.8.1 General Requirements and 7.8.3. Specific Requirements, sampling information and conditions are posted to the laboratory for review on the FACTS sample collection record.

7.8.6. Reporting Statements of Conformity

Statements of conformity reported on worksheets clearly identify:

- A. The results the statement applies to.
- B. Which specifications or standards were met, or not met.

7.8.7. Decision Rules

Statements of conformity to a specification or standard require the use of a decision rule to consider the uncertainty associated with method. Most decision rules used by ORS laboratories are documented in the compliance programs or standard methods. When the decision rule is not provided, the laboratory will use simple acceptance, where the acceptance level equals the tolerance level or customer requirements. Uncertainty measurements are available upon request.

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 34 of 46</p>

7.8.8. Reporting 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/or LIMS and may be recorded on the FDA form FD-465 as well. The laboratory classifications are defined in the FDA Data Codes Manual.

Records are maintained of conversations expressing opinions and interpretations about a sample with the customer.

7.8.9. Amendments to Reports

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 MAN-000044 ORA-LAB.5.10 Reporting Laboratory Data of Volume II. Amendments are to meet the same reporting criteria. Any changed information is clearly identified and where appropriate, the reason for the change is included in the report.

Related Procedures/References

- MAN-000044 ORA Lab Manual, Volume II, ORA-LAB.5.10 Reporting Laboratory Results.
- FDA Regulatory Procedures Manual.

7.9. Complaints

7.9.1. The ORS laboratories have a complaint process describing the handling of complaints received from any party. See MAN-000028 ORA-LAB.4.8 Complaints and Feedback. In addition to the resolution of these complaints, improvement in the area of concern is addressed and implemented in most cases.

7.9.2. The process for handling complaints is documented in MAN-000028 ORA-LAB.4.8 and is available to any interested party on the FDA internet site. The laboratory confirms whether the complaint relates to laboratory activities that it is responsible for and, if so, then addresses it.

7.9.3. The process for handling complaints includes the following:

- A. Description of the process for receiving, validating, investigating the complaint, and deciding appropriate actions to respond to it.
- B. Tracking and recording complaints, including actions taken to resolve

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 35 of 46</p>

them.

C. Ensuring appropriate action is taken.

7.9.4. The laboratory receiving the complaint will gather all information required to investigate, validate, address, and review the complaint and its outcome.

7.9.5. When possible, the laboratory will acknowledge receipt of the complaint, provide progress reports with the outcome of resolution, and formal notice of completion to the complainant.

7.9.6. Communications to the complainant is addressed in MAN-000028 ORA-LAB.4.8.

7.10. Nonconforming Work

7.10.1. The ORS laboratories have a control of non-conforming work procedure that is implemented when any aspect of their activities, 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:

- A. responsibilities and authorities for the management of identified non-conforming work to include taking actions such as the halting of work and/or the withholding of test reports based upon risk levels established by the laboratory
- B. actions are based upon the risk levels established by the laboratory.
- C. an evaluation of the significance of non-conforming work including an impact analysis on previous results and, if necessary, recall of work with notification to the customer
- D. remedial action taken, together with any decision about the acceptability of the non-conforming work
 - 1. The customer is notified if investigations show that non-conformances have affected work performed for or data reported to the customer. This notification is documented.
- E. responsibility for authorizing the resumption of work.

7.10.2. Records of nonconforming work and actions taken are maintained in QMiS.

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

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 36 of 46</p>

8.7 Corrective Action are promptly followed.

Related Procedures/References

- MAN-000029 ORA Laboratory Manual, Volume II, ORA-LAB.4.9 Control of Nonconforming Work

7.11. Control of Data and Information Management

7.11.1. ORS laboratories have access to the data and information needed to perform laboratory activities through various electronic records management systems including FACTS, LIMS, QMiS, and paper records maintained according to MAN-000032 ORA-LAB.4.13 Record and Data Management.

7.11.2. ORA information management system applications used for the acquisition, processing, recording, reporting, storage, or retrieval of data are validated prior to introduction by the FDA's Office of Information Systems Management.

If computer software is developed by the user, its development is authorized, documented in detail and algorithms are validated prior to implementation.

Changes to laboratory software configuration or modifications to commercial off-the-shelf software are also authorized, documented, and validated prior to use.

7.11.3. ORS laboratories have processes for the protection of data to include, but not limited to data integrity, data confidentiality during entry, collection, storage, transmission, and processing. The processes also ensure safeguards are in place to prevent unauthorized access to or amendment of records.

Information management system failures are recorded, and appropriate immediate and corrective actions are taken.

7.11.4. Laboratory information systems managed and maintained off-site meet all applicable requirements of ISO 17025:2017.

7.11.5. Instructions, manuals and reference data relevant to the laboratory information systems are readily available to personnel through the document control process (see section 8.3).

7.11.6. Calculations and data transfers are reviewed before the data is reported.

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 37 of 46</p>

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 7.7 Ensuring the Validity of Results.

8. Management System Requirements

8.1. Options

8.1.1. General

ORS laboratories have established, documented, implemented, and maintained a management system capable of supporting and demonstrating the consistent achievement of the requirements of ISO/IEC 17025:2017 to assure the quality of laboratory results. In addition to meeting the requirements outlined in sections 4 to 7 of this document the Standard requires ORS laboratories implement a management system in accordance one of the two following options.

8.1.2. Option A

ORS laboratories follow the requirements for option A, outlined in the following sections 8.2 to 8.9.

8.1.3. Option B

Option B of ISO/IEC 17025:2017 addresses minimal requirements for laboratories with a separate management system either certified to or at least structured to the requirements of ISO 9001. ORS laboratories do not fall within this category.

8.2. Management System Documentation (Option A)

8.2.1. 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". ORS laboratories are committed to providing testing that meets both the needs of the customers and the requirements of ISO/IEC 17025:2017 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.

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 38 of 46</p>

8.2.2. Commitments to Quality Issued by Director, Office of Regulatory Science

A. Good Professional Practice and the Quality of Testing

ORS laboratories are committed to the Standards of Ethical Conduct which define the obligations of public service issued under Executive Order 12674. Testing is conducted per the policies stated in Volume I, subsections 3 and this section. The laboratory management and personnel are committed to performing quality activities to assure integrity, accuracy, precision, reliability, and timeliness of the data.

B. Standard of Service

The laboratory's standard of service for the testing program is defined by the ISO/IEC 17025:2017 requirements, FDA regulatory needs included as part of the laboratory methods, and the following:

1. 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.
2. Sample handling and management procedures to maintain integrity of both the samples and the documentation to support the analytical data.
3. Maintenance of records in such manner that facilitates retrieving them later. Records are maintained in the analyst worksheet packet or web application by sample number. Records may be archived on- or off-site depending on the home division of the collector or in a web application. Archival retention periods are stated in the laboratory's record management procedure and are in accordance with the agency's established record retention schedule.
4. Employment of qualified and trained personnel to perform the tasks to support the laboratory objectives. Competency demonstrations by technical personnel conducting laboratory methods are conducted and documented.
5. 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.

<p align="center">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p align="center">Document Number: MAN-000025</p>	<p align="center">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p align="center">Page 39 of 46</p>

6. 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.

C. ORS 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.

D. The sections in this Volume describe elements and reference procedures that outline the management system established to accomplish the mission of the laboratory.

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

Primary consideration in all policies, procedures, and objectives is given toward retaining personnel competence and impartiality.

8.2.4. The policies for operation of the laboratory management system are established to address the requirements of ISO/IEC 17025:2017. ORS laboratories are committed to laboratory accreditation per the requirements of ISO/IEC 17025:2017.

The implementation of the quality policies is evidenced by the way 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.

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.

8.2.5. Management system procedures supporting quality policies are cited in the Related Procedures/References at the end of each section of this Volume. Where needed, each laboratory shall have procedures to implement the quality policies at the local level and include these procedures in the document control system. All documentation, processes, systems, records,

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 40 of 46</p>

related to the fulfillment of the requirements of ISO/IEC 17025:2017 shall be included in, referenced from, or linked to the management system.

- 8.2.6. All laboratory employees involved in laboratory activities have access to approved and controlled consensus standards, instrument manufacturers' manuals, and procedures for reference ensuring consistent application and validity of activities that contribute toward results reported.

8.3. Control of Management System Documents (Option A)

- 8.3.1. Changes to management system documents are made per the laboratory document control procedure and involve periodic revisions of this Volume.

- A. The operational procedures for ORS laboratories are controlled as described in MAN-000026 ORA-LAB.4.3 *Document Control and Management*.
- B. The document control and management procedure describes the process for controlling quality documents that form part of the laboratory 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.
- C. Control of electronic management system documents and data is addressed in section 7.11.

- 8.3.2. Document control requirements:

- A. Documents issued to personnel in the laboratory as part of the management system are reviewed for adequacy and approved by authorized personnel prior to issue in accordance with MAN-000026 ORA-LAB.4.3 Document Control and Management procedure.
- B. Documents are reviewed per an established schedule and revised as necessary to ensure continuing suitability and conformance with the management system and ISO/IEC 17025:2017 requirements. These reviews should include an assessment of reference documents and pertinent background information.
- C. Altered or new text is identified either in the document, document change history section, on a cover page, redline file, or in attachments. Changes can be described in general terms since the details can be demonstrated in the archived document. Document revision is recorded on each document and tracked within QMiS.

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 41 of 46</p>

- D. Authorized management system documents and external documents are available at locations where operations essential to the effective functioning of the laboratory are performed. Distribution and locale of these documents is controlled.
- E. A document control header as described in the document control and management procedure uniquely identifies management system documents generated by the laboratory. Such identification includes the revision status, identification number and inclusive pagination.
- F. The unintended use of obsolete documents is prevented, and suitable identification is applied to them if they are retained for any purpose.

8.4. Control of Records

- 8.4.1. ORS laboratories maintain records according to MAN-000032 *ORA-LAB.4.13 Record and Data Management* to sustain objective evidence showing fulfilment of the requirements of the quality system. These records are required to be legible and readily identifiable for retrieval.
- 8.4.2. Retention time, archival, and disposal of ORS Laboratory records are in accordance with SMG 3291.1 Records Management Policy and existing FDA and ORA record retention schedules.

Quality record storage and protection are maintained in QMiS or recorded within each laboratory’s individual records file plan.

Internal access to records is controlled through various methods, such as, but not inclusive of, password protected storage, both electronic and physical, provided to authorized personnel to maintain confidentiality. Access from entities outside FDA is governed by statutes within the Freedom of Information Act (FOIA) July 4, 1966, President Obama’s Freedom of Information Act Memorandum dated January 21, 2009, and Attorney General Holder’s Freedom of Information Act Guidelines, March 19, 2009.

Additional requirements regarding technical records are addressed in section 7.5 and control of electronic records is covered in section 7.11 of this document.

8.5. Actions to Address Risks and Opportunities

- 8.5.1. Top management in each ORS Laboratory meet regularly to assess risks and opportunities associated with all laboratory activities to:
 - A. Assure the management system achieves its intended results.

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 42 of 46

- B. Enhance opportunities to achieve the purpose and objectives of the laboratory.
- C. Prevent, or reduce negative impacts and potential failures in laboratory activities.
- D. Achieve improvement
- E. Examples of areas evaluated consist of the following, although the list is not all inclusive:
 - 1. Turnaround times for data reporting
 - 2. Training and competency
 - 3. Structure to ensure impartiality of personnel
 - 4. Equipment issues
 - 5. Program requirements
 - 6. Facilities/Environment
 - 7. Effectiveness of corrective and preventive actions
 - 8. Outcomes of internal audits
 - 9. Complaints
 - 10. Processes to ensure confidentiality

8.5.2. Plans, final evaluation, actions and implementation of actions, improvement, and assurance of intended actions are outlined in section 8.9 Management Reviews.

8.5.3. Actions taken to address risks and opportunities are proportional to the potential impact on the validity of laboratory results.

8.6. Improvement

8.6.1. 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 (see MAN-000031 ORA-LAB.4.12); the quality policy; and the quality objectives.

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

8.7. Corrective Actions

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 43 of 46</p>

- 8.7.1. Each ORS laboratory designates the authorities for implementing corrective action when one of the following is identified:
- A. non-conforming work,
 - B. departures from the policies and activities outlined within the management system, and
 - C. departures from required technical operations.
- 8.7.2. When a non-conformance is identified, the corrective action chosen addresses the magnitude of the non-conformance and the risk attributed to the non-conformance.
- A. Immediate action is implemented to correct a nonconformity and address the consequences..
 - B. An evaluation is performed to determine the cause(s), a history of similar issue(s), potential for recurrence, and the need for action to eliminate the problem to prevent recurrence.
 - C. Corrective actions are determined and implemented based upon this evaluation.
 - D. A review of the effectiveness of corrective actions is performed.
 - E. If necessary, updates for risks and opportunities are determined during planning.
 - F. Essential changes discovered during the corrective action investigation are implemented within the management system, where necessary.
- 8.7.3. Corrective actions are appropriate to the effects of the nonconformities encountered.
- 8.7.4. Corrective actions are recorded, to include the nature of the nonconformities, cause(s) and subsequent actions taken, including the results of any corrective action.

Related Procedures/References

- MAN-000030 ORA Laboratory Manual, Volume II, ORA-LAB.4.11 Corrective Action

8.8. Internal Audits

8.8.1. General

Internal audits are conducted according to a schedule included in the laboratory's audit procedure. Internal audits are conducted of activities to verify

<p style="text-align: center;">FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i></p>	<p style="text-align: center;">Document Number: MAN-000025</p>	<p style="text-align: center;">Revision #: 05 Revised: 14 Jun 2022</p>
<p>Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)</p>		<p style="text-align: center;">Page 44 of 46</p>

that operations continue to conform to the requirements of the management system and ISO/IEC 17025:2017.

An internal audit process is used to evaluate the effectiveness of the management system established for laboratory operations.

Note: The laboratory information management system is audited at least once per accreditation cycle.

8.8.2. Audit Program

- A. The internal audit program is defined in MAN-000033 ORA-LAB.4.14 Audits. The program takes into consideration the importance of the laboratory activities concerned, changes affecting the laboratory, and the results of previous audits.
- B. The QSM defines the audit criteria and scope for each audit in an audit plan.
- C. Results of the audits are reported to laboratory management.
- D. When audit findings cast doubt on the effectiveness of operations or the correctness or validity of the laboratory's test or calibration results, the laboratory implements appropriate correction and corrective actions in a timely manner according to MAN-000030 ORA-LAB.4.11 Corrective Action.
- E. The area of activity audited, the audit findings, and corrective action that arise from them are recorded according to the laboratory's audit procedure.

Related Procedures/References

- MAN-000033 ORA Laboratory Manual, Volume II, ORA-LAB.4.14 Audits.
- MAN-000030 ORA Laboratory Manual, Volume II, ORA-LAB.4.11 Corrective Action.

8.9. Management Reviews

A management review is conducted by the laboratory's executive management at least once each fiscal Year; however, can be conducted more often according to planned intervals determined by each ORS laboratory.

This review is conducted to ensure continuing suitability, adequacy, and effectiveness based upon information related to the inputs and outputs of laboratory activities and operations and stated policies and objectives.

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 45 of 46

Reviews of nonconforming work, personnel, and customer feedback are performed during management review to identify trends.

Related Procedures/References

- MAN-000034 ORA Laboratory Manual, Volume II, ORA-LAB.4.15 Management Review

9. Document History

Revision #	Status* (D, I, R)	Date	Author Name and Title	Approving Official Name and Title
2.0	R	5/2/2014	LMEB	LMEB
03	R	08/13/2019	LMEB	LMEB
04	R	01/22/2021	LMEB	LMEB
05	R	REFER TO QMIS	LMEB	LMEB

* - D: Draft, I: Initial, R: Revision

10. Change History

Revision #	Change
2.0	1.0– deleted “2005” 4.13, 4.14, & 4.15 e. – changed Sections 1300.1-1316.4 to Volume I, Section 1300 4.15 a. – deleted OPM manual reference and added OPM website 4.2.2 b. – added web application and added to last sentence on 3rd bullet 4.3.2.3 – revised 1st paragraph 4.13.1.2 – revised 4.13.2.1 – added “and/or LIMS” 5,8.3, 5.10.1., 5.10.2., & 5.10.5 – added reference to LIMS
03	All section numbering and content updated to reflect changeover from ISO/IEC 17025:2005 revision requirements to 2017 version requirements

FOOD AND DRUG ADMINISTRATION OFFICE OF REGULATORY AFFAIRS <i>Office of Regulatory Science</i>	Document Number: MAN-000025	Revision #: 05 Revised: 14 Jun 2022
Title: ORA Lab Manual Vol. I - Manual of Quality Policies for ORA Regulatory Laboratories (ORA-LAB.QM)		Page 46 of 46

Revision #	Change
04	5.6.5 and 5.6.6 – Added numbering to these two paragraphs and in 5.6.5, replaced “FDA Division of Ethics and Integrity” with the more generic “FDA procedures and policies” 7.8.2.2 – clarified that results in worksheets apply to the sample as received 7.8.6.1 – clarified the Decision Rule requirement with steps to take when a decision rule is not provided. 7.8.6.2 – Deleted Bullet C. 8.8.1 – Added AOAC requirement for internal audit of lab information management system. 8.9 – Added AOAC requirement for review of nonconforming work and other items during management review
05	Obsolete references have been removed. All remaining references and document ID numbers were updated to ensure adequate searches by FDA internal users within QMiS and links within document were verified or updated as needed for FDA internal users. Additions or Changes are highlighted within document. Reformatted.

11. Attachments

None