

	Standard Operating Procedure	SOP Number H-101	Revision 7
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Written by/ Date SS 11/04/21	Reviewed by/ Date K. Bunn 11/04/21	Approved by/ Date S. A. [Signature] 11/04/21	
Title: QC Laboratory Director	Title: Quality Systems Manager	Title: QA Manager	

1.0 Purpose

The purpose of this procedure is to describe the procedure for internal audits in order to ensure compliance with regulations and guidelines, as well as internal standards and policies. This includes but is not limited to monitoring the production, quality control, quality assurance, and other departments for compliance with cGMP, regulatory and product quality requirements. This SOP also includes the internal audit requirements to ensure that the LMS (Laboratory Management System) is effectively implemented and maintained and that LMS processes conform to planned arrangements, as well as to the requirements of ISO 17025.

2.0 Scope

This procedure applies to all internal audits conducted by/under the supervision of the Quality Assurance Department at Ion Labs, Inc. This procedure also describes procedures for the examination and verification of Ion Labs' technical operations for testing services.

3.0 Responsibility

- 3.1 It is the responsibility of the QA department to coordinate internal audits, review the internal audit reports, schedules for appropriateness, and ensure that scheduled audits are conducted.
- 3.2 It is the responsibility of Department Managers and assigned personnel to provide access to their facilities at the auditor's request, respond to internal audit reports in a timely manner, and ensure that improvement action plans are developed, adopted, and implemented in their respective departments.
- 3.3 QA is responsible for ensuring any contracted auditors performing internal audits are appropriately qualified. When contracted auditors perform internal audits, contracted auditors may assume the duties of QA, except for approval of the internal audit schedule, assignment of corrective action and follow-up activities.
- 3.4 Management shall review all findings and actions related to Internal Audits and ensure that improvement action plans are implemented and effective. This review shall be documented during the annual Management Review.

4.0 Definitions

- 4.1 **QA** – Quality Assurance
- 4.2 **OTC** – Over-The-Counter; Nonprescription drug product
- 4.3 **CFR** – Code of Federal Regulations
- 4.4 **GMP** – Good Manufacturing Practices
- 4.5 **CAPA** –Corrective and Preventive Action

5.0 References

- 5.1 C-502, SOP, Document Retention, Storage, and Destruction
- 5.2 F-506, SOP, Facility Maintenance and Sanitation
- 5.3 H-101-F1, Form, Internal Audit Report Form
- 5.4 QS-108, SOP, Corrective and Preventative Action
- 5.5 21 CFR Parts 111, 117, 201, 210, 211, 701 - as applicable to Dietary Supplements, Cosmetics and OTC

6.0 Procedure

- 6.1 Auditor Competence for Laboratory Audits
 - 6.1.1 Only qualified Internal Auditors conduct internal audits on the LMS. Such qualifications for internal resources appear in the Auditors' Training Records. Auditors' training records reflect that they are qualified to perform audits based on successfully completing auditor training, which includes:
 - ISO 17025 Orientation or ISO 17025 Awareness Training
 - Audit theory
 - Audit techniques and methods
 - Checklist generation
 - Reporting findings

6.2 Audit Scheduling, Frequency and Requirements:

6.2.1 An internal audit schedule shall be maintained throughout the year to ensure that elements within the quality system requirements as elaborated in FDA's regulation for Dietary Supplements, Cosmetics and OTC Products are audited on a regular basis and at a minimum of once a year. Activities are audited more frequently if required. The Internal Audit function may be satisfied -in combination of, an annual 3rd Party Audit that is conducted at Ion Labs, resulting in an accredited nationally / internationally recognized certification, Customer Quality System Audits or various Facility GMP Audit Assessments (e.g. Monthly Sanitation / GMP Audits -Ref. SOP F-506, Food Defense Plan Facility Audit -Ref. SOP QS-109). These audits combined must meet, at a minimum - applicable 21 CFR requirements or related governmental requirements and documented Internal Audit Process and procedure.

6.2.2 Internal Audits may consist of a review of various operational functions to include Good Manufacturing Practices in Manufacturing, Testing, Packaging, Labeling, Quality Related or Holding and Distribution Operations for Dietary Supplements as outlined in 21 CFR Part 111. Also, as applicable for all aspects of Cosmetic and OTC Manufacturing, Testing, Labeling, Packaging, Holding and Distribution as outlined in the CFR.

6.2.3 All processes or areas that affect the Lab's provision of testing services are internally audited to provide information on whether the laboratory activities and defined processes conform to the LMS policies and procedures, to the requirements of ISO 17025, and to determine their effective implementation and maintenance. The audit includes observation of testing activities. Internal auditors are encouraged to identify any opportunities for improvement, as well as evidence where improvements have been made. Internal audits are planned to meet any contractual requirements, and as required by QA.

6.2.3.1 QA maintains the Internal Audit Schedule to ensure internal audits are conducted at planned intervals. QA schedules audits taking into consideration the importance of the laboratory activities concerned, changes affecting the laboratory as well as the results of previous audits. The entire laboratory management system is audited at least once per year (at the system level). Technical audits are also scheduled at least annually.

6.2.3.1.1 The laboratory audits consist of two categories: procedural and technical. Procedural audits may be performed at a different time than technical audits. The audits for both

categories are performed in accordance with the Internal Audit Schedule.

- 6.2.3.1.2 Each accredited test method (or potential accredited method) and work area is audited for compliance with the pertinent test method or work instruction.
 - 6.2.3.1.3 Technical audits generally consist of observations (by the auditor) of test procedures and comparison of the observations with criteria documents. Documents, reports, data packages, and training files as appropriate are reviewed during the audit.
 - 6.2.3.1.4 Criteria documents can consist of analytical methods, contractual documents, or published government regulation, if applicable. Recent nonconforming work incidents and/or corrective actions may also serve as criteria.
 - 6.2.3.1.5 Data packages are reviewed for compliance with laboratory and customer requirements. The data packages are traced throughout the entire testing process, beginning with the assessment of the project, and ending with reporting.
 - 6.2.3.1.6 Internal audits of a specific process or procedure can be requested by Management at any time. Requests are scheduled through the Quality Manager. Other areas of interest might be included in the requested audit at the discretion of the Quality Manager.
 - 6.2.3.1.7 Internal audits can be announced or unannounced at the discretion of the Quality Manager.
- 6.2.3.2 When performing an audit in the laboratory, all general laboratory safety protocols must be followed. These include, but are not limited to, the use of personal protective equipment.
- 6.2.4 The Internal Audit Schedule shall be developed at the beginning of the year by the QA Department in consultation with management, based on the status and importance of activities covered by the quality system. The Internal Audit Schedule may be reviewed/modified throughout the year (quarterly) to accommodate for new product types or the influx of various audits which may suffice for that respective quarterly audit. This will be evaluated by Quality Management. All aspects of operations will be monitored as they relate to

Dietary Supplements, Cosmetics, as well as OTC items (see Attachment 1 for example).

6.3 Unannounced Internal Audits or 3rd Party Audits may occur at any time. Audit Response and Corrective and Preventive Actions will be provided at the direction /timeline dictated by the Auditor. Audit Structure

6.3.1 The Internal Audit will be performed by trained auditors which may consist of a cross functional team ensuring participation and ownership of the program or as an independent audit conducted by the QA Manager or designate.

6.3.2 Training may consist of formal Auditor Training from a certified, reputable service or program that is developed internally. This training will be documented.

6.3.3 Audits will be carried out by personnel who are independent of the area they are auditing. Personnel conducting internal audits must be qualified and must have knowledge of GMP regulations, company's quality system and procedures.

6.4 Audit Preparation

6.4.1 The QA department shall coordinate the schedule for the audit with the Department Manager /3rd Party Auditor/Customer Lead Auditor to ensure, if possible, that the audit does not conflict with operational commitments of the unit being audited. Auditors may audit their own work as long as they can ensure the objectivity of the audit results. Where possible, they do not audit their own work.

6.4.2 Prior to the internal audit, the auditor(s) should review records of completed corrective and preventative actions, and past audit findings for the department to be audited, then develop a checklist covering the quality system elements and activities to be audited in line with applicable 21 CFR (see Attachment 2 for example) or applicable ISO 17025 requirements

6.4.3 QA audit checklist can be used as an aide to check that all the topics relevant to the area have been examined. The use of the checklist, when combined with a well-structured approach, helps ensure all relevant topics are reviewed in the time available.

Note: The checklists only serve as a guide to the auditor(s). Other areas may be investigated as deemed necessary by the internal auditors based on audit observations or as requested by QA or management.

6.4.4 QA may contract LMS internal audits to qualified external resources. In this case, LMS audits will be planned on the basis that the contractor will complete a full audit compliant with this procedure. The audit will be planned as deemed appropriate by QA. Planning for the audit may also include an agreed approximate date for the next year's audit. More detailed audit planning documents such as a detailed schedule will be provided in advance of the audit. QA and the contractor will discuss where to focus the audit and information regarding previous audit findings (including accreditation assessments) as well as influences resulting from considering the importance and status of the management system.

6.4.4.1 The contractor will provide evidence that they are competent to audit (e.g., formal qualification [IRCA, Exemplar Global, ASQ] or substantial experience auditing) and have some experience in the industry. Having helped with the implementation of a laboratory management system is considered adequate experience. Some knowledge and experience of ISO 17025 and sector schemes will also be required and may be demonstrated by formal qualification (e.g., IRCA or Exemplar Global, ASQ) or experience working with the standard.

6.4.4.2 Checklists, audit evidence, audit reports, findings lists, etc., generated by the contractor may be of their own design so long as they meet the general requirements of this procedure.

6.4.4.3 Any relevant documents, including past audit reports and audit criteria (e.g., uncontrolled copies of current procedures or test methods and requirements) are provided to the contract auditor(s).

6.5 Audit Execution

6.5.1 Auditor(s) will conduct the audit in accordance with the schedule (or as an unplanned audit) and document audit findings. Auditors receive information through several sources such as but not limited to the following:

6.5.1.1 Interviews with personnel

6.5.1.2 Examination of documentation

6.5.1.3 Observation of activities and conditions

6.5.1.4 Review of quality and technical records

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6.5.2 The interviews should be conducted in the work area, if possible or appropriate, so that actual processes can be observed and any records or related data will be available for review. Information obtained from the interview as well as the records and site inspection shall be documented. The records review will most typically be conducted before conducting interviews and physical inspections with follow-up reviews conducted following the findings of previous steps.

Note: Although audits should take place during normal working hours, the audit shall be conducted with the minimum interruption of departmental operations.

6.5.3 When a nonconformance or observation is identified, the auditor presents the nature of the nonconformity/observation and the evidence to the personnel involved for verification, clarification, and addresses any questions or concerns that the personnel may have, as well as to give advice, when requested, regarding any problems which are uncovered. Notes made in the audit checklists should support any observations or nonconformities determined. QA reviews the report and nonconformances to ensure that they are complete and properly written. QA or the Lab Director initiates corrective action for each valid nonconformance.

6.5.4 Audit observations severe in nature may be escalated to the CAPA System at the discretion of Quality Management.

6.6 Audit Wrap-up Meeting

6.6.1 After any audit session, a wrap-up/close-out meeting will be conducted to discuss the non-conformity observations and recommendations to verify or modify them, and get more information from audited personnel.

Note: The wrap-up meeting provides the audited department with an opportunity to voice any objections. It is important that this opportunity is taken to clear up any misunderstandings and to explain any limitations on the performance of the audit. If valid objections are raised, the audit team should review the objections thoroughly and take necessary action.

6.6.2 The department personnel together with the auditor(s) will determine the course of action to improve compliance with the applicable regulations and guidelines.

6.7 Internal Audit Report

6.7.1 Within fifteen (15) working days of completing the internal audit, the auditor/

team prepares an internal audit report. Form H-101-F1 Internal Audit Report Form is completed to reflect any observations noted during the audit. The respective departments where the observations apply -shall review the report and complete form H-101-F1 sections for: corrective actions/plan, responsible person(s), due date (within 20 days unless approved by QA Manager or designee), and inform the auditor(s)/ QA department within ten (10) working days of receiving the audit report about any other issue not covered in the report, request an extension or present a plan for timely completion. The Audit report will reflect the observation(s) and corrective and preventive actions taken. Close-out of the report/form may be extended due to change in processes, equipment or noted plan.

6.7.2 Copies of the report may be distributed to management and department management, as appropriate, for review. The original report, audit checklist, and any other supported documents are kept by the QA department and Document Control as required by SOP C-502 Record Storage, Retention, and Destruction.

6.8 Follow Up to Corrective Actions

6.8.1 All corrective actions documented as a result of an Internal Audit shall be documented in Form H-101-F1.

6.8.2 According to the proposed completion date, QA department, or internal auditor, or designee conducts a follow-up review to verify the completion of agreed-upon management actions and ascertains the status of any open recommendations.

6.8.3 When all corrective actions have been implemented and observations are completed, the auditor or designate will verify effectiveness and close out the audit.

6.9 Results of Laboratory Management System internal audits are submitted for Management Review. Internal Audit Reports may be submitted in their entirety, or a summary of audit results and findings may be developed for submittal to top management.

7.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	06/09/10	New	-	-
1	04/04/13	Updated SOP format and number. Made the SOP more detailed and to be in compliance with 21 CFR part 111	13-274	V. Itcheva
2	04/16/14	Updated SOP format. Added CAPA reference. Added reference to cross-functional teams.	14-0326	S. Millar
3	02/22/15	Added OTC requirements. Added 3 rd Party Audits. Added reference to Management Review.	15-0087	S. Millar
4	04/10/17	Biennial review: added reference to CAPA program/procedure.	17-0391	S. Millar
5	04/18/18	Added formal Auditor Training for overseas auditor by certified service or program. Added QC Laboratory Internal Audit to be performed monthly. Added QC Laboratory Internal Audit Checklist format as an attachment.	18-0137	L. Erickson
6	01/21/19	Changes include the reflection of Cosmetics throughout the document. CFR reference added. Removed reference to/QC Laboratory Internal Audit Checklist (Attachment 3). Defined audit types that may suffice for Internal Audits. Added reference to 3 rd Party unannounced audits.	19-0068	S. Millar
7	11/04/21	Added requirements for ISO 17025:2017.	CC-21-0414	J. Sassman

8.0 Attachments

- 8.1 Attachment 1 – Example of Internal Audit Schedule
- 8.2 Attachment 2 – Example of Audit Checklist Format

Attachment 1 – Example of Internal Audit Schedule



201x Internal Audit Schedule

Area Audited	Scope 21 CFR Part XXX/Guidance Document/or related Regulatory Reference	Scheduled Audit (Y or N)	Date Opened	Date Closed

Attachment 2 – Example of Audit Checklist Format



Checklist for Internal Audit

Area Audited

Date:

<i>Reg. Section</i>	<i>Procedure Referenced</i>	<i>Areas of Audit</i>	<u><i>Adequate</i></u> <u><i>Y or N</i></u>	<i>Comments</i>
Audit Notes: Random Logs, Forms and Documents were sampled during the audit to ensure compliance with those respective procedures				
Audit Recommendations:				
Documents Reviewed:				
Doc. No./Logs	Document Name			Revision/Effective

Auditor Signature and Date: _____

