ION LABS	Standard Operating Procedure **Core Quality Systems and Quality Events**	**SOP Number** **QS-112**	**Revision** **1**
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Written by/ Date	**Reviewed by/ Date**	**Approved by/ Date**
06/20/22	06/20/22	06-20-22
Title: QC Laboratory Director	**Title: Quality Systems Manager**	**Title: VP of Quality & Regulatory Affairs**

1.0 Purpose

This procedure provides an overview of Core Quality System(s) (CQS) used to manage cGMP activities and the events that trigger these quality systems.

2.0 Scope

This procedure only applies to CQS listed in Table 1 and provides instructions common to each of these systems. Separate SOPs as referenced in Table 1 provide details necessary for execution of each CQS / Event Type.

3.0 Responsibility

3.1 It is the responsibility of Directors, Managers and Supervisors to:

3.1.1 Understand that the CQS defined herein exist and are necessary in circumstances defined in Table 1.

3.1.2 Refer to additional procedures defined in Table 1 as necessary when working with a CQS for a specific event type.

3.2 It is the responsibility of Directors, Managers, and Supervisors assigned to initiate or complete documentation of an event to:

3.2.1 Follow the instructions defined in this procedure.

3.2.2 Have documented training for procedures defined in Table 1 specific to events assigned.

3.2.3 Refer to additional procedures defined in Table 1 as necessary when executing a specific CQS for an event type.

3.3 It is the responsibility of Document Control / Quality to:

3.3.1 Assign and log event numbers.

3.3.2 Assign event due dates.

3.3.3 Approve or reject requests for event numbers.

3.3.4 Approve or reject event due date extensions, event cancellations, and/or event revisions.

3.3.5 Approve or reject event closures.

3.3.6 It is the responsibility of the Training Department to:

3.3.6.1 Provide New Hire and Annual refresher training regarding the procedures established within this SOP to all New Hire and existing employees.

4.0 Definitions

4.1 **DC** – Document Control

4.2 **CQS** – Core Quality System(s) is a system (i.e. Standard Operating Procedure (SOP) or combination of SOPs) that handle and manage a quality event and that are within the scope of this SOP as defined in Table 1. NOTE: There are Quality Systems outside the scope of this SOP that handle Quality Events; however, they do not meet this definition of CQS.

4.3 **Quality Event** – An event that triggers the use of a CQS and that is subject to cGMP regulations.

4.4 **cGMP** – Current Good Manufacturing Practices as defined by regulations associated

with the manufacture, testing, holding, etc. of a food, dietary supplement, drug product, or device manufactured by Ion Labs.

4.5 **OOS** – Out of Specification –a result for a test performed does not meet established acceptance criteria.

4.6 **OOT** – Out of Trend – a result for a test performed that meets established acceptance criteria, but is not statistically consistent with historical trends.

4.7 **AR** – Aberrant Result – a result for a test performed that meets established acceptance criteria, but is considered atypical, abnormal, anomalous, deviant, irregular, questionable, or unexpected.

4.8 **Adverse Event** – Any health-related event associated with the use of a cosmetic, dietary supplement, or OTC that is adverse.

4.9 **Serious Adverse Event** – Results in death, a life-threatening experience, inpatient hospitalization, a persistent or significant disability or incapacity, a congenital anomaly/birth defect, or one that requires medical or surgical intervention to prevent such serious outcomes.

4.10 **Non-Conforming Result (NCR)** - any end value or result that does not meet a pre-established specification or expectation.

5.0 References

5.1 QS-112-F1, Form, Quality Event Extension Request

5.2 QS-112-F2, Form, Quality Event Cancellation Request

5.3 QS-112-F3, Form, Quality Event Amendment Request

5.4 A-118, SOP, Management Review of Quality Metrics

5.5 C-502, SOP, Record Storage, Retention, and Destruction

5.6 D-105, SOP, Out of Specification/Out of Trend Investigation

5.7 C-201, SOP, Deviation and Investigation Procedure

5.8 QS-108, SOP, Corrective and Preventive Action (CAPA)

5.9 QS-113, SOP, Effectiveness Checks (EC)

5.10 QS-101, SOP, Complaints

5.11 QS-102, SOP, Adverse Events

5.12 C-403, SOP, Change Control Procedure

5.13 C-105, SOP, Protocol and Report Document Requirements

5.14 QS-114, SOP, Quality Risk Management

5.15 D-126, SOP, Non-Conforming Results in the QC Laboratory

6.0 Procedure

6.1 CQS / Event Types

6.1.1 The table below (Table 1) lists all quality event types subject to this SOP and provides reference to detailed instructions for processing each type.

Table 1

CQS / Event Type Code	Event Type Name - CQS / Event Type Description	CQS SOP Reference
INV	**Investigation** – This CQS manages the investigation of laboratory results that are OOS. This procedure also allows the investigation of results that are OOT or AR.	D-105
DEV	**Deviation** – This CQS manages both planned and unplanned deviations from procedures, batch records, and nonconformities related to products, materials, equipment, processes, quality systems, etc. Handle nonconformities associated with OOS or OOT lab results using the INV CQS.	C-201

CQS / Event Type Code	Event Type Name - CQS / Event Type Description	CQS SOP Reference
CAPA	**Corrective Action Preventative Action** – This CQS tracks progress and completion of CAPA associated with other applicable event types. The most common triggers for this CQS are INV and DEV events.	QS-108
EC	**Effectiveness Check** – This CQS provides a mechanism and feedback loop to check the effectiveness of executed CAPA. When a CAPA requires follow-up for effectiveness this CQS is required.	QS-113
COMP	**Complaint** – This CQS manages the processing of complaints received about manufactured products and is triggered when a complaint is received.	QS-101
AE	**Adverse Event** – This CQS manages the processing of adverse events and is triggered when a complaint is received that meets the definition of an adverse event.	QS-102
CC	**Change Control** – This CQS manages changes to cGMP documents, systems, equipment, software, etc. The CQS is triggered when Ion Labs personnel requests an applicable change.	C-403
PRTCL	**Protocol** – This CQS tracks and manages various types of protocols used to govern non-routine processes. Ion Labs personnel use this CQS when they request a protocol.	C-105
RPT	**Report** – This CQS tracks and manages various types of reports. Ion Labs personnel use this CQS when they request a report.	C-105
NCR	**Non-Conforming Result** – This CQS manages any non-conforming result that meets the definition as a minor category.	D-126

6.2 Events with impact to multiple CQS

6.2.1 If an event would trigger more than one CQS, the event must be documented in each applicable quality system with the following exceptions:

6.2.1.1 Investigations / Deviations

6.2.1.1.1 If a documented investigation discovers that an OOS is a result of a deviation, document the deviation within the investigation system. A separate deviation event is not required.

6.2.1.1.2 If a documented deviation generates an OOS, document the OOS within the deviation system. A separate investigation event is not required.

6.2.1.2 {Complaints or Adverse Events} / {Investigation or Deviation}

6.2.1.2.1 If a customer complaint or adverse event discovers either an OOS or a deviation not previously discovered / documented, then document the deviation and/or OOS investigation within the complaint system. A separate deviation and/or investigation event is not required.

6.2.2 While the exceptions listed above do not require duplicated documentation within the listed events, it is acceptable to initiate an event for each CQS impacted.

6.3 Event Numbers

6.3.1 DC is responsible for assigning a unique number for each quality event applicable to this procedure. DC will assign numbers using the following format:

6.3.1.1 [Event Type] – [Year] – [####]

6.3.1.2 Where:

6.3.1.2.1 [Event Type] – Use the event type code characters defined in Table 1 for the event type.

6.3.1.2.2 [Year] – Use the last two digits of the year the event started/opened.

6.3.1.2.3 [####] – A sequential number representing the count of numbers assigned to that event type for the given year starting at 0001.

6.3.2 Table 2 below provides example event number.

Table 2

Example	Event Number
The third deviation issued in 2018	DEV-18-0003
The fifth investigation issued in 2019	INV-19-0005

Note: The term "event number" is a generic reference to the number assigned to an event as defined here. A more specific reference to a specific type of event number (i.e. deviation number, change control number, etc.) may be used interchangeably with the term "event number" in documentation that references or discusses these numbers (i.e. SOPs, Protocols, Reports, cross references on documentation, etc.) For example, reference to a specific deviation can reference the number as "event number – DEV-18-0003" or as "deviation number DEV-18-0003."

6.4 Event Log

6.4.1 DC will maintain a spreadsheet of each event issued and event number. At a minimum, the following information will be maintained in the log:

6.4.1.1 Event number

6.4.1.2 Event revision (if applicable)

6.4.1.3 Event Title / Description

6.4.1.4 Event logged by Initials / Date

6.4.1.5 Event cancellation – This is left blank unless the event is actually cancelled

6.5 Event Initiation / Closure

6.5.1 Each CQS has forms specific to associated events that are used to initiate and close those events.

6.5.2 DC will assign event numbers, and update the event log upon completion and approval applicable initiation form(s).

6.5.3 DC will close events upon completion and approval applicable closure form(s).

6.6 Due Dates and Extensions

6.6.1 Each quality event is assigned a due date. Closure of an event on or before the assigned due date IS NOT a requirement for compliance. Due dates are assigned as a process management tool and to provide management with information about how various individuals and departments are able to adhere to assigned due dates. If an event is closed after an assigned due date, a deviation is not required.

6.6.2 Quality may choose to open a deviation if a delay in closure of an event poses a significant risk to safety or compliance.

6.6.3 Default due dates are defined in Table 3. Assign the default due date if reasonable. Each situation may require either more or less time. For example, if the event closure is necessary to minimize risk to a product or cGMP system, then assign a shorter due date. Conversely, if time is required to close the event, then allow that time with a longer due date.

Table 3

Event Type Code	Default Due Date
INV	30 days from open
DEV	30 days from open
CAPA	30 days from open
EC	90 days from implementation
COMP	45 days from open
AE	45 days from open
CC	30 days from open
PRTCL	30 days from open
RPT	30 days from open
NCR	30 days from open

6.6.4 After assignment of a due date, circumstances may prevent completion of an event on time. If there is a justified need for an extension, use form QS-112-F1 Quality Event Extension Request to request a new due date.

6.6.5 An extension IS NOT required just because an event is closed after an assigned due date.

6.6.6 DC will update due dates based on approved extensions, and will track the number of times a due date is extended.

Note: The quality department tabulates events that are open and past due and provides them for consideration during the monthly management review of quality metrics. Additionally, the number of times an event is extended is reviewed. Refer to SOP A-118 Monthly Review of Quality Metrics. This procedure provides a mechanism to provide awareness and resources and to set priorities to close quality events.

6.7 Event Cancellation

6.7.1 Cancel Events using Form QS-112-F2 Event Cancellation Request. This form provides the mechanism for the event owner to provide justification of the cancellation and for DC to approve the cancellation. DC will not approve the cancellation of an event without an acceptable justification.

6.7.2 DC will initial and date the cancellation of the event in the event log upon approval of the cancellation request.

6.8 Event Amendment / Revision

6.8.1 In the circumstance that a quality event has been closed but needs to be amended or revised a new revision of that quality event will be made and logged just like a new event of that type, but will use the same event number with an incremented revision number.

6.8.2 Initiate an event amendment / revision using Form QS-112-F3 Event Amendment Request.

6.8.3 DC will log each event revision into the same event log used for that event type. Treat the amendment / revision as a new event with respect to open, due, and

closed dates.

6.8.4 Each initial quality event will be given a revision number of 0, while any following revision number will increase sequentially for each new revision.

6.8.5 Add additional documentation to the original event documentation and use good documentation practices when correcting original documentation.

6.8.6 Use fresh forms from the original CQS to amend/revise the documentation as applicable. For example, use a blank form used to close a deviation to document approval of the revision. Alternately, memorandums, letters, reports, etc. may be used to approve the revision; however, the same level of approval or higher used to approve the original event is required for any revisions (i.e. same departments represented and same managerial levels or higher represented).

6.9 Record Management

6.9.1 DC will maintain original event documents.

6.9.2 DC will scan completed event documents and file electronically.

6.9.3 Maintain records as defined in SOP C-502 Record Storage, Retention, and Destruction.

6.9.4 Issue copies of event documentation to subject records as applicable. For example, file a copy of a deviation or investigation with the subject batch record. Mark / Stamp official copies with the word "Copy" on the first page of the copy.

7.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	12/30/19	New procedure.	N/A	K. Burris
1	06/08/22	Added NCR scope to procedure. Changed responsibility section. Updated forms.	CC-22-0259	J. Sassman