1.0 Purpose

This procedure establishes the requirements for the issuance and tracking of cGMP protocols and reports at Ion Labs, Inc.

2.0 Scope

This procedure applies to all protocols and reports generated at Ion Labs, Inc. unless the protocol or report is not a cGMP document, or if the protocol or report is covered by a more specific procedure.

3.0 Responsibility

3.1 All persons writing, reviewing and approving a protocol or report are responsible for assuring content is consistent with the requirements established in this procedure and that it is complete and thorough.

3.2 All protocol reviewers and approvers are responsible for ensuring that the content applicable to their particular area of expertise or discipline is appropriate with regard to approach, methods, procedures, and analysis. Reviewers/approvers must conduct reviews in a timely manner and provide appropriate feedback and comments.

3.3 Quality is responsible for ensuring that document content is consistent with this procedure as part of the review and approval of the document.

4.0 Definitions

4.1 **DC** – Document Control

4.2 **BPR** – Batch Production Record

4.3 **IQ** – Installation Qualification; a formal assessment of the means of accommodating new equipment and testing its materials

Example: IQ should ensure that necessary utilities, space. etc. are available for the equipment, and that the equipment is made of the materials specified.

4.4 **OQ** – Operational Qualification; a formal challenge of equipment parameters

Example: If equipment must operate in specific ranges, those should be verified.

4.5 **PQ** – Performance Qualification; similar to OQ but tested under load

Example: If equipment must operate in specific ranges, those ranges are measured while in use with materials.

4.6 **Validation** – The formal documentation of demonstrating that a method, system, or process will consistently operate within pre-described parameters and are suitable for the intended use

4.7 **Verification** – The formal demonstration that a validated method, system, or process is suitable for a specific application that may vary slightly from the parameters used for validation (e.g. a different but similar product). Verification activities are usually a sub-set of the activities carried out for validation

4.8 **SOP** – Standard Operating Procedure

4.9 **DC** – Document Control

4.10 **cGMP** – Current Good Manufacturing Practices

4.11 **CQS** – Core Quality System

5.0 References

5.1 C-105-F1, Form, Protocol and Report Initiation Request

5.2 C-105-F2, Form, Protocol and Report Closure Request

5.3 C-201, SOP, Deviation and Investigation Procedure

5.4 QS-112, SOP, Core Quality Systems and Quality Events

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

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

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

6.0 Procedure

6.1 Protocols

6.1.1 Protocols define processes, execution steps, expected outcomes, limits, acceptance criteria, etc. for cGMP activities not otherwise defined by SOPs, Batch Records, Test Methods, Specifications, etc. Protocols may be used for non-cGMP activities in accordance with this procedure at the discretion of Quality Management.

6.1.2 Typical activities requiring the use of a protocol include but are not limited to the following:

6.1.2.1 Validation / Verification of a cGMP process, system, or method

6.1.2.2 Reprocessing of products or materials

6.1.2.3 IQ/OQ/PQ of equipment, instrumentation, systems, software, etc.

6.1.2.4 See also Section 6.3.4 to assign protocol numbers to documents authored by individuals and organizations outside of Ion Labs.

6.1.3 Protocol Record Management

6.1.3.1 Original pre-approved protocols are maintained by DC.

6.1.3.2 If required for execution, DC will issue a controlled copy of the pre-approved protocol.

6.1.3.3 Controlled copies used for execution will be returned to DC upon completion and will be maintained with the original pre-approved protocol, or with the BPR if necessary.

6.1.3.4 Documentation/data generated and/or collected during the execution of a protocol must be filed with the protocol and/or subsequent report(s). Typically it is attached to the protocol report(s).

- Reprocessing protocols and all documentation generated during its execution will be maintained in the BPR, with the completed protocol document.

6.2 Reports

6.2.1 Reports summarize information and document conclusions and decisions impacting cGMP activities not otherwise defined by SOPs, Batch Records, Test Methods, Specifications, etc. Reports may be used for non-cGMP activities in accordance with this SOP at the discretion of Quality Management.

6.2.2 Typical activities requiring the use of a report include but are not limited to the following:

6.2.2.1 Summary of the execution of a protocol governed by this SOP.

6.2.2.2 Reports of and responses to audits / inspections by customers, third party auditors, and government agencies.

6.2.2.3 See also Section 6.3.4 to assign report numbers to documents authored by individuals and organizations outside of Ion Labs.

6.2.3 All conclusions made in reports must be based on objective review of the data and observations made during the execution of the protocol.

6.2.4 Final reports must explain any deviations from associated protocols or other pre-established and approved criteria that occurred and the impact these deviations have on the integrity of the study.

6.2.4.1 When deviations from acceptance criteria or approved specifications are observed, these must be investigated to the degree necessary to understand why the deviation occurred and the impact of that deviation.

6.2.4.2 A report may use SOP C-201 Deviation and Investigation Procedure and the associated forms to document a deviation, and then reference the deviation number in the report.

6.2.4.3 A report may document a deviation in the body of the report instead of using SOP C-201 Deviation and Investigation Procedure and the associated forms as long as the same principles established in C-201 Deviation and Investigation Procedure are applied.

6.2.5 Report Record Management

6.2.5.1 Original approved reports are maintained by DC.

6.2.5.2 Documentation/data generated and/or collected during the execution of a protocol must be filed with the protocol and/or subsequent report(s). Typically it is attached to the protocol report(s).

6.3 Requirements Common to Protocols and Reports

6.3.1 Document Format

6.3.1.1 The format of a protocol and/or report will vary based on the type of study being conducted or reported, its complexity, and objectives. DC may have templates available from previously executed protocols or reports.

6.3.1.2 Some protocols are written with space provided to document the execution of the protocol (i.e. blanks to fill in). If the document is intended to serve as both a protocol and a report, only a protocol number will be assigned. See section 6.4 for assignment of numbers.

Documents that serve this dual purpose (protocol and report) must have the following features:

- Pre-Approval Signatures
- Post-Approval Signatures
- A mechanism to document deviations from the protocol.
- A place to reference additional documentation as applicable.

6.3.2 Content

6.3.2.1 Protocols and reports have similar content sections. There are a few content sections listed here that only apply to one or the other which is explained in the list below.

6.3.2.2 Protocol / Report Number and Pagination

- The protocol / report number assigned to the document should be on the front page of the document. Include this number on the header or footer of each page along with pagination of pages. Attachments do not need to be paginated, and the protocol / report number does not need to be on each page of the attachments. See Section 6.3.3 for additional requirements for attachments.

6.3.2.3 Introduction / Scope / Purpose

- One or more of these sections should be used as applicable. In general it is important to explain why the protocol / report exists. Cross-references to events or circumstances that created the need for the document should be provided. Specifically if a deviation, investigation, etc. is the reason for the document, then reference the specific event number. If the document pertains to a specific system or piece of equipment then the system or equipment should be specified including applicable identification numbers.

6.3.2.4 Rationale

- If applicable, provide explanation and / or justification for the approach taken or for the conclusions drawn.

6.3.2.5 Procedure

- The procedure defines what must be done (in a protocol) or what was done (in a report). It must be detailed enough for the reader to achieve or repeat the intended purpose. The procedure section may reference other documents (i.e. batch records, SOPs, previous protocols, etc.) rather than repeat information unnecessarily.

6.3.2.6 Acceptance Criteria

- The Acceptance Criteria section defines what limits that must be achieved if a protocol is considered successful. If a report is used to summarize a protocol, then the acceptance criteria should be included or referenced in the report. Acceptance criteria may not be necessary in a report depending upon the nature of the report.

6.3.2.7 List of Attachments

- Any documents necessary to support the protocol or report must be listed within the document so that a reader will be able to discern whether or not all required attachments are present. It is best to include this section with an entry of "none" if there are no attachments needed to support the document.

6.3.2.8 Signatures

- At least two signatures are required for each protocol or report. At least one signature must be from the author of the report. At least one signature must be from the Quality department. If multiple departments are significantly involved in the execution of the

protocol and /or are impacted by the results in a report, then at least one signature from each of these departments should be present.

Note: Additional signature requirements listed in section 6.3.1.2 above.

6.3.3 Attachments

6.3.3.1 Must be properly identified with a reference to the specific protocol and/or report number to which they are related.

6.3.3.2 Must be listed within the protocol and/or report as a list of attachments.

Note: Reprocessing protocols do not require this information to be added to normal BPR pages used to document reprocessing activities. Only supplemental pages for reprocessing will have this information added and listed in the protocol as an attachment.

6.3.4 Protocols / Reports authored outside of Ion Labs

6.3.4.1 If a protocol or report is authored by a 3rd party service provider, auditor, customer, or government agency, those reports are not likely to meet requirements defined by this SOP.

6.3.4.2 Ion labs personnel may write an internal protocol or report to provide the necessary content and supply the outside report as an attachment to the document written internally. The internal document may be minimal and reference the attachment for the majority of the content.

6.4 Protocol or Report Initiation / Closure

6.4.1 Initiate a protocol or report by submitting form C-105-F1 Protocol and Report Initiation Request to DC.

6.4.2 Close a protocol or report by submitting form C-105-F2 Protocol and Report Closure Request to DC.

6.5 Additional Requirements from QS-112 Core Quality Systems and Quality Events

6.5.1 This procedure is considered a CQS that is also controlled by SOP QS-112 Core Quality Systems and Quality Events.

6.5.2 The term "event" is a generic reference to any of the CQS covered by SOP QS-112 Core Quality Systems and Quality Events. The term "event" is used interchangeably with specific CQS events as applicable (i.e. either "protocol" or "report" here).

6.5.3 SOP QS-112 Core Quality Systems and Quality Events provides instructions common to all Ion Labs CQS including the following topics which are not to be duplicated here:

- Assignment of unique event numbers (i.e. Protocol and Report numbers)
- Logging of events DC
- Assignment of event due dates
- Event due date extensions
- Event cancellations
- Event revisions / amendments
- Monitoring of open events
- Record management and retention instructions

7.0 Revision History

Revision	Date	Description of Changes	CCN	By
0	05/07/10	New procedure.	-	-
1	09/28/12	Made general reorganization to provide clarification, changed SOP title, expanded protocol type and protocol number, made protocol number assignment and all issuing and maintenance activities the responsibility of DC	12-0145	V. Iltcheva
2	10/03/14	Scheduled review: updated SOP format.	14-0777	V. Iltcheva
3	01/07/19	Scheduled review: removed paper log. Added requirements for electronic log. Added new categories for protocol numbers. Removed obsolete information. Corrected formatting. Changed SOP number. Added reference to C-501.	19-0021	K. Burris
4	01/16/20	Added reference to QS-112. Added protocol due date. Removed protocol numbering system.	19-0602	K. Burris
5	06/03/22	Updated logo, formatting, and title. Clarified documentation requirements for reprocessing protocols. Updated throughout for uniformity to other procedures.	CC-22-0254	K. Burris

ION LABS	Protocol and Report Initiation Request		
	Form: C-105-F1	CCR No. CC-22-0254	Revision: 1

EVENT INFORMATION

Protocol / Report Number		**Revision #**	
Protocol / Report Title / Description			

EVENT TYPE

☐ PRTCL - Protocol	☐ RPT - Report

EVENT DATES

Protocol / Report Open Date

Protocol / Report Due Date

PROTOCOL / REPORT – OWNER (I.E. ASSIGNED TO)

COMMENTS

Name	Title	Signature	Date
Completed By: (Author)			
Assignment Accepted By: ☐ **N/A if same as completed by**			
Approved By: (Quality)			

ION LABS	Protocol and Report Closure Request		
	Form: C-105-F2	CCR No. CC-22-0254	Revision: 1

EVENT INFORMATION

Protocol / Report Number		**Revision #**	
Protocol / Report Title / Description			

DATE INFORMATION

Closed Date	

CLOSURE SUMMARY

Include as applicable: Evidence and/or statement of closure, cross references to supporting documentation, general conclusions / outcome, etc.

Name	**Title**	**Signature**	**Date**
Completed By: (Author)			
Approved By: (Quality)			