	Standard Operating Procedure Ensuring the Identity, Purity, Strength and Composition of Liquid Form Finished Products	SOP Number A-119	Revision 3
		Effective Date 09/14/21	Page Page 1 of 10
Written by/ Date 08-04-21	Reviewed by/ Date 08/04/21	Approved by/ Date 08-23-21	
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1.0 Purpose

The purpose of this procedure is to describe all stages of manufacturing, packaging, labeling, testing and holding of Liquids, Lotions, Creams, and Serums to ensure the identity, purity, strength and composition of each product.

2.0 Scope

This procedure applies to all liquid form finished products manufactured at Ion Labs, Inc.

3.0 Responsibility

3.1 It is the responsibility of all departments – Production, R&D, QA, QCS, QCL, Purchasing, Shipping, and Receiving to strictly follow this procedure.

4.0 Definitions

4.1 **Identity** – A specific unique characteristic of a product; a positive match (complies) between an established/standardized characteristic and a finished product attribute

4.2 **Purity** –Absence of impurities

4.3 **Strength** – Concentration of listed component

4.4 **Composition** – Appropriate list of ingredients and components in finished product

4.5 **Quality** – Means that the finished product consistently meets the established specifications for identity, purity, strength and composition, and has been manufactured, packaged, labeled, tested, and held under conditions to prevent adulteration

4.6 **QC** – Quality Control

4.7 **LC** – Label Control

4.8 **R&D** – Research and Development

4.9 **PO** – Purchase Order

4.10 **CoA** – Certificate of Analysis

4.11 **RMP** – Raw Material Profile

4.12 **RMID** – A unique identifying number assigned to each raw material

4.13 **R#** – A unique identifying number assigned to individual batches of raw materials upon receipt

4.14 **RMSTT** – Raw Material Specification and Test Ticket; A document that lists test methods, specifications, results and information for each unique raw material

4.15 **MBR** – Master Batch Record; a compilation of documents and forms that identifies all of the pertinent instructions, processes, and specifications necessary to manufacture a product

4.16 **BPR** – Batch Production Record; an accurate reproduction of the MBR issued to production

4.17 **Product Profile** – Establishes a products components, in-process, finished product specifications, and stability which ensure the identity, purity, strength, and composition of the product

4.18 **FPTT** – Finished Product Test Ticket; an internal CoA

4.19 **CCP** – Critical Control Point; a point during production of a product at which controls are applied and adherence to specification is determined prior to proceeding

4.20 **IAV** – Ingredient Addition Verification and Results Form; Document containing specifications associated with label claim support

4.21 **OTC** – Over the Counter; medicines sold directly to a consumer without a prescription from a healthcare professional.

5.0 References

5.1 A-108, SOP, Good Manufacturing Practices and Personal Hygiene

5.2 B-401, SOP, Liquid Mixing Tank

5.3 B-604, SOP, LPS Liquid Overflow Filler

5.4 B-904, SOP, Packaging Procedure

5.5 C-103, SOP, Batch Production Record Review and Release of Finished Product

5.6 C-104, SOP, Master Batch Record and Issuance of Batch Production Record

5.7 C-707, SOP, Critical Control Point Specifications

5.8 D-702, SOP, Density Determination of Liquids

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

5.10 D-403, SOP, Calculations for Ingredient Addition Verification for Finished Products

5.11 D-901, SOP, Raw Material Life Cycle

5.12 D-902, SOP, Establishment of Specifications

5.13 E-204, SOP, Receiving Process for Raw Materials

5.14 E-601, SOP, Vendor Qualification

5.15 E-702, SOP, Finished Product Sampling Procedure

5.16 E-703, SOP, Raw Material Sampling

5.17 E-704, SOP, AQL Statistical Sampling Plan

5.18 E-802, SOP, Quarantine of Materials

5.19 21 CFR Part 111

5.20 21 CFR Part 211

5.21 21 CFR Part 700

6.0 Procedure

6.1 Purchasing of Raw Materials

6.1.1 All raw materials used in the manufacturing of Liquids/Lotions/Creams must be purchased from qualified suppliers, approved by Ion Labs and must be listed on the Approved Vendors List as per SOP E-601 Vendor Qualification.

6.2 Receiving, Inspection, Sampling, testing and release of Raw Materials

6.2.1 Receiving of Raw Materials

6.2.1.1 Purchasing will make available in Batchmaster approved POs to warehouse personnel.

6.2.1.2 The warehouse associate compares incoming materials to the packing list and Batchmaster item description. The warehouse will quarantine material that does not match the PO for quality, grade or vendor. Quality will be notified of the discrepancy and determine the suitability of the material.

6.2.1.3 Warehouse associate assigns a sequential number in the format of R00001 to each incoming raw material, creates a label containing the RMID, raw material name, R number, vendor name, and vendor lot number for the raw material container, and applies to each bulk container of raw material (refer to SOP D-901 Raw Material Life Cycle, SOP E-204 Receiving Process of Raw Materials, and SOP E-802 Quarantine of Materials).

6.2.2 Inspection and Sampling of Raw Materials

6.2.2.1 QC samples raw materials according to SOP E-703 Sampling of Raw Materials and E-704 AQL Statistical Sampling Plan.

6.2.2.2 The samples will be delivered to the lab for analysis along and logged into the QC laboratory sample log book (Refer to SOP E-703 Sampling of Raw Materials.)

6.2.3 Testing and Release of Raw Materials

6.2.3.1 QC Lab completes the testing of raw materials as outlined in the RMP based on the CoA Challenge Status, and documents the results on the RMTS (Refer to SOP D-901 Raw Material Life Cycle).

Note: Data generated for the first component of a partial shipment can be used for the second component release in instances when partial shipments are received, each with the same manufacturer lot # and separate R#s are generated. A separate RMTS will be generated for the second component of the partial shipment for tracking purposes.

6.2.3.1.1 Raw materials that meet the release specification listed in the RMP can be processed for release. QC lab updates the raw material status in Batchmaster to "Released". (Refer to SOP D-901 Raw Material Life Cycle and SOP E-802 Quarantine of Materials/ Products).

Note: All approved RMs that are used in Ion Labs products are subject to CofA challenges as defined in SOP D-901 Raw Material Life Cycle and must pass verification testing if the RMs are to be used in Ion products. All raw materials require three CofA challenges before reduced testing can be implemented.

6.2.3.1.2 For raw materials that do not meet the release specifications listed in the RMP, the QC lab will update the raw material status in Batchmaster to "Hold" until a final disposition has been made by Quality Management (Refer to SOP D-105 Out of Specification/Out of Trend Investigation and SOP E-802 Quarantine of Materials/Products).

6.3 Production and Process Control System

6.3.1 Master Batch Record and Issuance of Batch Production Record

6.3.1.1 R&D creates Product Profile, prepares the Master Formula, Weighing and Blending Instructions, and Supplement Facts Sheet for each unique Formula to ensure uniformity in the finished batch (refer to SOP C-603 New Product Realization Process).

6.3.1.2 The BPR issued to production, accurately follow the appropriate MBR and all steps in the manufacturing of the batch (Refer to SOP C-104 Master Batch Record and Issuance of Batch Production Record).

6.3.2 Manufacturing Operations

Note: All manufacturing operation must be conducted under conditions and controls that protect against the potential for growth of microorganisms and the potential for contamination.

Only plastic pallets are permitted inside manufacturing areas where raw materials and product are exposed. Wooden pallets are only allowed in packaging rooms when preparing shipping boxes. Wooden pallets are only allowed in the warehouse, hallways and areas where material and product are not exposed. All wooden pallets must be heat-treated and marked "HT".

The personnel must be garbed appropriately with frocks and/or disposable lab coats, shoe covers and/or dedicated shoes as applicable, hair nets, beard covers, safety glasses and gloves (refer to SOP A-108 Good Manufacturing Practices and Personal Hygiene).

Identify all processing lines and major equipment used during manufacturing to indicate their contents, including the name of the lotion/cream/serum and the specific batch number.

Each stage of the manufacturing process should be approved or rejected by QC personnel.

6.3.2.1 Weighing and Blending Process (Refer to SOP B-901 Weighing and Blending Procedure).

6.3.2.1.1 A QC inspection of the room, equipment, balances, and utensil cleanliness must take place prior to any weighing and blending. The inspection must be documented on the BPR.

6.3.2.1.2 Before weighing a raw material, the following must be verified by the operator and QC inspector and the verification recorded in the BPR:

- Check the RMID against the BPR.
- Check the description of the material against the BPR.
- Ensure the material has been released by QC.
- Check the expiration date of the material.

6.3.2.1.3 During the weighing, the following steps should be observed:

- Tare the scale to read zero between each weighing step.
- The R # of each raw material must be documented in the BPR.
- Each step of the weighing process should be checked by a second production person and/or QC inspector as per BPR.

6.3.2.1.4 During the blending, the following steps should be observed:

- Place the weighed raw materials into the mixing tank, following the instructions on the BPR.
- Each step of the blending process must be checked by a second production person and/or QC as per BPR.
- After the blending process QC inspector performs CCP 6 Liquid/Lotion/Cream Tank Sampling. QC Lab will perform CCP 6 testing and QC will provide startup approval based on lab results before blended lotions, creams, or serums can be transferred to the filling department. (Refer to SOP C-707 Critical Control Point Specifications).
- If the blend is approved, QC will release the blend for the next manufacturing stage.
- If the blend is not approved, Quality and R&D will be notified of the failure.

6.3.2.2 Packaging Process (Refer to SOP B-904 Packaging Procedure)

6.3.2.2.1 Prior to the beginning of the packaging process, the container(s) containing the lotions, creams, or serums and all packaging components must be inspected by QC personnel for the correct product, batch number, and packaging. They should be released and approved by QC personnel. This has to be documented in the BPR.

6.3.2.2.2 A QC inspection of the packaging area, equipment, utensil and scale(s) must take place prior to the beginning of packaging process. The inspection must be documented on the BPR.

6.3.2.2.3 The packaging procedure stated in the BPR must be strictly followed.

6.3.2.2.4 Packaging operator performs four bottle checks at the beginning and every 30 minutes until the end of the packaging process for product quality.

6.3.2.2.5 QC performs four bottle checks at the beginning and every one hour until the end of the packaging process for product quality. Interval based inspections can be adjusted as needed based on risk (refer to SOP B-905 Quality Control Inspection Process).

- Verify the fill weight and ensure that the product is free from foreign material and consistent in color
- CCP-7 Liquid/Lotion/Cream Weight Verification

6.3.2.2.6 The labels must be issued by Label Control and must be the correct labels for the job. The product label used must be affixed on the appropriate space(s) in the BPR before the beginning of the labeling process and signed by QC personnel.

6.3.2.2.7 The labeling instructions stated in the BPR must be strictly followed.

6.3.2.2.8 Packaging operator performs four bottle checks at the beginning and every 30 minutes and at the end of the labeling process for product quality.

6.3.2.2.9 A QC Inspector performs four bottle checks at the beginning and every hour until the end of the labelling process to ensure product quality. Intervals can be adjusted as needed based on risk (refer to SOP B-905 Quality Control Inspection Process)

6.3.2.2.10 At the completion of packaging, QC inspector should submit to QC Lab reserve samples and stability samples (if required). (Refer to SOP E-702 Finished Product Sampling Procedure).

6.3.2.2.11 The pallet(s) with packaged product/bulk should be properly identified with product name, customer name, batch number, pallet(s) number and quantity. QC will place a "Hold-Pending Release" tag on each pallet and product should be moved to designated area holding for QC test results and release by QC department (Refer to SOP E-802 Quarantine of Materials/ Products).

Note: All components and lotions/creams/serums should be held under appropriate conditions of temperature, humidity, and light so that the identity, purity, strength, and composition of the components and lotions/creams/serums are not affected.

6.3.2.3 Finished Product Testing and Release

6.3.2.3.1 QC inspector takes the test samples/micro samples to the laboratory for analysis and logs them in the QC laboratory sample log book.

6.3.2.3.2 QC Lab is responsible for testing all finished products in accordance with SOP D-902 Establishment of Specifications.

6.3.2.3.3 QC Lab performs the specified testing in accordance with applicable laboratory method standard operating procedures and documents in a laboratory notebook or on the appropriate forms (Refer to section D SOPs Laboratory Operations and Specifications).

6.3.2.3.4 At the completion of testing, QC Lab enters the results of the testing on the Method Specific Test Tickets and Finished Product Test Ticket – Internal CofA.

6.3.2.3.5 Any finished product testing failures [i.e. Out of Specification (OOS) results] are investigated per D-105 Out of Specification/Out of Trend Investigation.

6.3.2.3.6 QC supervisor/designee will review the entire BPR to ensure that it is complete, all required information is entered or attached, and all the signatures/ dates are in place and will make a final disposition (Refer to SOP C-103 Batch Production Record Review and Release of Finished Product).

- If the product is released, Quality Systems will notify applicable departments and a warehouse associate will remove the "Hold- Pending Release" tag.

- If the product is rejected, QC should change the "Hold- Pending Release" tag to a "QC Hold" tag on a pallet and move the pallet to the designated area until further investigation is performed and finalized.

7.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	11/10/16	New	16-0607	L. Titolo
1	12/07/16	Changed title. Aligned protocol to reflect process for all liquid form finished products manufactured at Ion Labs.	16-1115	B. Johns
2	05/01/20	Updated outdated definitions and references, update procedure to include the use of Batchmaster, edit language for clarity, edit to be consistent with current practices.	CC-20-0318	S. Sassman
3	08/04/21	Removed reference to FPSS added reference to FPTT.	CC-21-0306	C. Mitchell