

	Standard Operating Procedure	SOP Number B-901	Revision 12
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Written by/ Date <i>[Signature]</i> 06/15/23	Reviewed by/ Date <i>[Signature]</i> 06/20/23	Approved by/ Date <i>[Signature]</i> 06/20/23	
Title: Warehouse Manager	Title: Senior VP of Operations	Title: Quality Assurance Director	

1.0 Purpose

The purpose of this procedure is to establish a process for blending of powder raw materials.

2.0 Scope

This procedure applies to blending of powder raw materials at Ion Labs, Inc.

Responsibility

- 3.1 It is the responsibility of all personnel involved in the blending of powder raw materials to follow this procedure.
- 3.2 It is the responsibility of the department manager/supervisor to implement this procedure and to ensure that all involved personnel are adequately trained.
- 3.3 It is the responsibility of QC to inspect and ensure that this procedure is being followed.

4.0 Definitions

- 4.1 **BPR** – Batch Production Record
- 4.2 **QC** – Quality Control
- 4.3 **R Number** – Receiving Number; a unique identifying number assigned to raw materials upon receipt
- 4.4 **RMID Number** – Raw Material Identification Number
- 4.5 **FIFO** – First In, First Out; an inventory plan that ensures that items purchased first will

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be used first. Raw materials, components, drug related products, containers, and closures approved for use shall be rotated so that the oldest approved stock is used first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.

- 4.6 **Allocation** – The process of identifying materials in inventory and selectively placing them for use in a batch

5.0 References

- 5.1 C-707, SOP, Critical Control Point Specifications
- 5.2 A-108, SOP, Good Manufacturing Practices and Personal Hygiene
- 5.3 QS-106, SOP, Allergen Control
- 5.4 A-107, SOP, Workplace Safety Procedure
- 5.5 F-510, SOP, Sharp Instrument Control Procedure
- 5.6 C-201, SOP, Deviation and Investigation Procedure
- 5.7 B-111, SOP, Cleaning of Manufacturing/Production Areas and Equipment
- 5.8 B-103, SOP, Small Parts Cleaning and General Sanitation
- 5.9 B-104, SOP, Floor Drain Cleaning and Sanitizing Procedure
- 5.10 E-101, SOP, Warehouse and Inventory Control

6.0 General Requirements

- 6.1 Ensure that the blending room and blender are clean and that the appropriate cleaning log books have been filled out.
- 6.2 Ensure that the blending room is clear of all evidence of the prior batch, including the BPR, raw materials, and in-process materials.

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- 6.3 Ensure that scale calibration is verified daily and that the designated logbook has been filled out.
- 6.4 Check the scale calibration sticker to ensure that the scale calibration has not expired. Report expired calibration to QC personnel. Do not use expired calibration equipment.
- 6.5 Identify the blending room with the correct product name and batch number.
- 6.6 A QC inspection of the room, equipment, balances, and utensil cleanliness must take place prior to bringing any raw materials into the room. The inspection must be documented in the BPR.
- 6.7 Personnel and visitors must follow good manufacturing practices as per SOP A-108 Good Manufacturing Practices and Personal Hygiene. Personnel must follow safety precautions by wearing appropriate personal protective equipment as outlined in SOP A-107 Workplace Safety Procedure.
 - 6.7.1 Personnel must be garbed appropriately with company frocks and/or lab coats, hairnets, shoe covers and/or dedicated shoes (as applicable), beard covers (if applicable), dust masks, gloves, and safety glasses.
 - 6.7.1.1 Gloves must be a minimum thickness of 0.08mm for the blending area. This should help to prevent contamination of the blending materials due to ripped gloves during the weighing and blending process.
- 6.8 Raw Materials containing Allergens: Ensure proper utensils are used and frocks/lab coats are worn during the handling/processing of any allergen materials as defined in SOP A-108 Good Manufacturing Practices and Personal Hygiene and QS-106 Allergen Control to eliminate any chance for cross contamination. Frocks and lab coats must be changed after allergen usage. Ensure a proper clean has been performed prior to the start of any blending of raw materials containing allergens.
- 6.9 A material allocation report is required for every blend. This report must accurately reflect all raw materials that are intended for the batch and the expiration date of each

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material.

- 6.10 A lead or supervisor will verify all weighed out material is accurate and correct and will sign the “all materials have been verified prior to loading the blender”.

Note: If the material description or RMID number does not match what is specified in the BPR, contact QC and Production Management. QC will place a hold tag on the material in question and isolate it from the remaining raw materials. Do not proceed until QC or Production Management indicates that it is acceptable to proceed.

- 6.11 During the blending process, the following steps should be observed:

- 6.11.1 Place the weighed raw materials into the blender, following the instructions in the BPR.

Note: Prior to the “ON” and “OFF” operation of the v-blenders, the operator must attach the safety barricade that will not allow entrance past the yellow caution marking identified across the door while the equipment is in operation.

Note: All associates must adhere to the safety barricade, caution markings, and door cautions while equipment is in operation.

- 6.11.2 Each step of the blending process must be checked by a second production employee.

7.0 Procedure

- 7.1 Retrieve the batch record (to confirm what manufacturing room will be used) and allocation sheet.
- 7.2 Ensure that the cleaning log has been filled out AND approved by QC prior to bringing any materials into the room.

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- 7.3 Fill out the in-process tag for both doors of the blending room.
- 7.4 Bring the raw materials into the blending room.
- 7.5 Review the batch record to ensure that all steps are correct and all items are accounted for. Also review for what equipment is needed for the batch.
- 7.6 Gather all necessary supplies. At a minimum, the following supplies will be needed:
 - 7.6.1 Hygrometer
 - 7.6.1.1 Ensure that the hygrometer calibration has not expired.
 - 7.6.2 Scoop
 - 7.6.3 Tape gun
 - 7.6.4 Marker
 - 7.6.5 Pen
 - 7.6.6 Zip ties
 - 7.6.7 Box cutter
 - 7.6.7.1 Follow SOP F-510 Sharp Instrument Control Procedure for proper assignment and maintenance of blades.
 - 7.6.8 Scissors
 - 7.6.9 Bags
 - 7.6.10 Snips
 - 7.6.11 Weigh-out bin
 - 7.6.12 Scale(s)

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7.6.12.1 Ensure that the scale calibration has not expired. Following SOP G-207 Calibration Verification and Operation of Scales, verify the calibration and document in the calibration log book.

- 7.7 Verify container count against the BPR recorded by the weighing team.
- 7.8 Stage all raw materials for any premixes that are required per the blending instructions (hand screen, oscillate, or blender mixes). Once staged the premixes may be completed.

Note: Remove and discard all desiccant pouches found in the raw material packaging.

- 7.9 Stage the remaining raw materials for addition to the blender. All raw materials MUST be transferred into drums prior to loading the blender.

7.9.1 The only exception to the transfer are raw materials that are stored in pails. For these items, cut the security lock and zip tie, and fold the inner bag over the pail rim.

- 7.10 Label all drums with the raw material item number or the Premix number.
- 7.11 Follow the blend instructions exactly as outlined in the BPR. Deviations to the instructions as outlined (except for additional material screening) must be managed through deviation. Refer to SOP C-201 Deviation and Investigation Procedure.
- 7.12 While the blend is in-process, prep the drums needed for blend discharge. Drums are to be prepped with two food-grade liners, the first bag a thin liner and the second bag a thick liner. Super sacks with a thick liner may be used in place of drums, as needed and approved by Management.
- 7.13 For Ribbon blenders only, a dead spot purge is required. Empty one drum from the discharge valve and add back to the top of the blender. Do this until the blend is uniform.
- 7.14 Before discharging the blend, initiate an in-process label recorded with the product name and lot number and tag the drums with the labels, along with an orange quarantine tag.

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7.15 Equip the discharge valve with either a 14-mesh or 10-mesh screen and drop enough of the blend into a container (or super sack) until the container is half full. Inspect the powder for clumpy aggregates (the material is not flowing freely through the screen). If clumpy aggregates are noted, contact the blending lead or supervisor for instruction.

7.16 If the blend flows freely through the screen and no clumps are noted, change to 4-mesh screen and discharge the remainder of the blend into the prepped containers. Wrap the top of the liner and close the container with a tight-fitting lid.

Note: For some products, large desiccant bags should be placed into the drums during closure of the containers. Follow instructions outlined in the BPR.

7.17 Calculate the net weight of each drum using the following calculation:

$$7.17.1 \text{ Gross Weight} - \text{Tare Weight (6.70kgs)} = \text{Net Weight}$$

7.18 Enter the weight on the BPR Weigh and Mix Order. Record the line number of the container weight on the in-process label located on the container for the associated line.

7.19 Once the weight of all containers has been calculated, add all container weights to find the total blend weight. This number will be documented on the Blending Master Reconciliation page, in the Transfer Out column. The numbers must be confirmed by a second blending operator (or equivalent).

7.20 Sweep up any fallen powder on the floor and weigh it to get the total waste amount. Add this weight to the Weigh and Mix sheet, and also to the Master Blending Reconciliation page, in the Waste column.

7.21 Complete all required calculations on the Master Blending Reconciliation and have a second blender confirm these calculations. Once confirmed, the blending section of the BPR can be closed. Complete all required calculation on the Master Blending Reconciliation in the BPR and notify a QC inspector to perform CCP 1 - Blending (Absence of Foreign Material and Bulk Density) to ensure blend uniformity, to determine that the blend conforms to specifications, and to make a disposition decision. Refer to

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SOP C-707 Critical Control Point Specifications.

7.21.1 QC will label the drums that pass with a release sticker and blending personnel will move the drums into the blending release area.

7.21.2 QC will label the drums that fail with a hold sticker and move the drums into the QC Hold area.

Note: All product holding drums must be wiped down with IPA on the outside of the drum and the lid to remove excess powder prior to removing from the blending and compression areas.

7.22 After blending, cleaning of the blending room and equipment should be performed and properly documented according to the appropriate cleaning and equipment procedures.

8.0 Revision History

Revision	Date	Description of Changes	CCR #	By
1	04/26/13	New procedure.	-	-
2	08/19/13	Added section 3.5, added in section 5.7, added section 5.7.1, 5.8, Note, removed section 5.12, added section 5.13, 5.14, 5.14.1, 5.14.2.	13-702	V. Ilcheva
3	03/13/14	Added instructions to place partial raw materials into secondary confinement. Updated SOP format. Changed QA to QC, added FIFO.	14-0182	L. Titolo
4	04/29/14	Added instructions for allergen materials.	14-0340	S. Millar
5	03/30/15	Added notes in section 6.11.	15-0297	K. Burris
6	01/27/16	Added note in section 6.6. Added note in section 6.7. Added requirement for two food grade liners to be placed in drums. Added instruction for 1 st batch FTIR blend pulls.	15-0555	P. Zittere
7	03/10/16	Added reference to cutting instruments and knives.	16-0218	S. Millar
8	04/30/18	Added note to remove desiccant from raw materials prior to use. Removed FTIR sample pull requirements.	18-0152	L. Erickson
9	05/18/21	Complete rewrite and organization of procedure to outline current processes.	CC-21-0187	K. Burris
10	10/07/21	Added step 6.7.1.1 to specify glove requirements.	CC-21-0375	K. Burris
11	10/21/22	Updated procedure to reflect new weighing and dispensing process.	CC-22-0227	J. Murphy
12	06/15/23	Add lead/supervisor verification to weighed out material prior to loading the blender.	CC-23-0311	J. Murphy

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