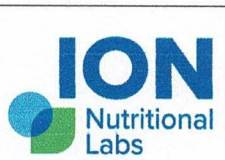
<table>
<tr><td rowspan="2">  </td><td rowspan="2">Standard Operating Procedure
Using Raw Materials at Risk</td><td>SOP Number
D-302</td><td>Revision
1</td></tr>
<tr><td>Effective Date
05/10/24</td><td>Page
Page 1 of 7</td></tr>
<tr><td colspan="2">Written by/ Date
03/25/24</td><td>Reviewed by/ Date
03/26/24</td><td>Approved by/ Date
03-26-24</td></tr>
<tr><td colspan="2">Title: QC Laboratory Manager</td><td>Title: Chief Operations Officer</td><td>Title: VP of Quality & Regulatory Affairs</td></tr>
</table>

1.0 Purpose

The purpose of this procedure is to describe the requirements necessary to use a raw material prior to complete quality release.

2.0 Scope

This procedure will be applied to those raw materials that have not completed the required laboratory testing and have not been released for use. This procedure will define the risk categories associated with unreleased raw materials and will define minimal testing required to be approved for at risk use.

3.0 Responsibility

3.1 It is the responsibility of QC Laboratory Management to complete form D-302-F1 RM High Risk Assessment for Potential Release for Use at Risk for any material intended for use at risk in production activities prior to completion of all testing required by normal release of that material.

3.2 It is the responsibility of QC Laboratory Management to maintain a High Risk material List as outlined in this procedure.

3.3 It is the responsibility of DC to approve assessments on D-302-F1 RM High Risk Assessment for Potential Release for Use at Risk and file this document with RM release documentation.

3.4 It is the responsibility of DC to review the release status of all RM used in manufacturing processes and ensure that all RM are fully released before releasing any Finished Product batches.

4.0 Definitions

4.1 **At Risk –** state of which using a raw material prior to full laboratory release. Using raw materials at risk is further divided into the below risk levels:

4.1.1 **Low** – expected to have minimal to no impact for its use prior to full laboratory release

4.1.2 **Medium** –expected to have the potential for finished product impact for its use prior to full laboratory release

4.1.3 **High** – expected to have increased potential for finished product impact for its use prior to full laboratory release and generally not recommended to use prior to full laboratory release

4.1.4 **Prohibited** – present the potential for significant impact to the quality of any finished product in which it will be used; cannot be used prior to full laboratory release without the approval of operational and executive management

4.2 **Raw Material Classification –** based on the form that the raw material is received as described below.

4.2.1 **Botanical Powder** – complete powder form of any plant

4.2.2 **Botanical Extract** – created by soaking the botanical in a liquid that is able to retrieve certain chemicals or beneficial parts of the plant to be used in a product; may or may not be received on a carrier ingredient

4.2.3 **Chemical Excipient** – inactive material that aides in the processing of a formulation

4.2.4 **Vitamin or Mineral** – active ingredient, natural or synthetic, that are typically the main components of any formulation; low percentage vitamins or minerals may or may not be received on a carrier ingredient

4.3 **DC** – Document Control

4.3 **OOS** – Out of Specification

4.4 **QC** – Quality Control

4.5 **R#** – Receiving Number; a unique identifying number assigned to raw materials upon receipt

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

4.7 **RM** – Raw Material

4.8 **COA** – Certificate of Analysis

5.0 References

5.1 C-601, SOP, New Product Approval Process

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

5.3 E-601, SOP, Vendor Qualification

5.4 D-901, SOP, Raw Material Life Cycle and COA Challenge Process

5.5 D-902, SOP, Establishment of Specifications

5.6 D-302-F1, Form, RM Risk Assessment for Potential Release for Use at Risk

5.7 D-302-F2, Form, Prohibited Risk RM List

6.0 Raw Material Risk Classification

6.1 Low Risk raw materials will generally meet these qualifications:

6.1.1 Raw material supplier is fully analytically qualified, i.e. three lots have been successfully C of A challenged per D-901 Raw Material Life Cycle and COA Challenge Process.

6.1.2 Raw material type does not present any significant safety concerns, i.e. microbial or heavy metal contamination.

6.2 Medium Risk raw materials will generally meet these qualifications:

6.2.1 Raw material supplier is fully analytically qualified.

6.2.2 Raw material is required to meet specific physical characteristics to ensure the finished product is able to be successfully processed in manufacturing, i.e. particle size, density, form.

6.3 High Risk raw materials will generally meet these qualifications:

6.3.1 Raw Material has not been fully analytically qualified.

6.3.2 Raw material has the potential to impact the safety of finished product.

6.4 Prohibited Risk raw materials will generally meet these qualifications:

6.4.1 Raw materials that have failed to meet all release specification on past receipts are Prohibited risk. If a specific root cause was identified for the failure, then it is possible to consider removal of the material from the Prohibited Risk list, but only if the root cause is managed sufficiently to eliminate the failure.

6.4.2 Raw materials that are inherently unstable are Prohibited risk. Some materials will degrade or change under transport and/or storage conditions. If these changes have the potential to significantly impact the material, then classify that material as Prohibited risk.

6.4.3 Any raw material that is the first time receipt.

7.0 Raw Materials Characteristics

7.1 Botanical Powders (High Risk)

7.1.1 Typically not processed to remove contaminants such as heavy metals.

7.1.2 May or may not be treated to reduce microbial contaminates.

7.1.3 Critical testing – ID, micro, heavy metals.

7.2 Botanical Extracts (Medium Risk)

7.2.1 Typically processed to extract components of interests. This extraction process may reduce the amounts of potential contaminants that will be present in the extracted material.

7.2.2 Extraction process typically reduces the microbial load of the material.

7.2.3 May require strength testing to support a label claim.

7.2.4 Critical testing – ID, Strength (if applicable).

7.3 Chemical Excipients (Low Risk)

7.3.1 Typically synthetically created.

7.3.2 Potential for contaminants present is significantly reduced.

7.3.3 Minimal laboratory testing required for release.

7.4 Active Ingredients (Low Risk)

7.4.1 Typically vitamins and/ or minerals.

7.4.2 Potential for contaminants present is significantly reduced.

7.4.3 Usually requires strength testing to support a label claim.

8.0 Procedure

8.1 Initiate a risk Assessment

8.1.1 If production operations require access to a raw material before normal laboratory release testing of that material is completed, initiate form D-302-F1 RM Risk Assessment for Potential Release for Use at Risk and complete Phase 1 portion.

8.1.2 The risk questions and assessment process are also summarized in a flow chart format presented in Attachment 1.

8.1.3 Decision questions located on Form D-302-F1 RM Risk Assessment for Potential Release for Use at Risk will determine the requirements necessary for the use of any material at risk.

8.1.4 Proceed to Phase 2 portion of Form D-302-F1 RM Risk Assessment for Potential Release for Use at Risk.

8.1.5 Phase 1 and Phase 2 must both be completed prior to using any raw material at risk.

8.1.6 Form D-302-F1 RM Risk Assessment for Potential Release for Use at Risk will be archived with each individual raw material upon completion and release.

8.2 Prohibited Risk Material List

8.2.1 The QC Laboratory will maintain form D-302-F2 Prohibited Risk Raw Material List.

8.2.2 Assess new raw materials for risk during the specification creation for those materials.

8.2.3 Update the Prohibited Risk Raw Material list after OOS results for a material are confirmed.

8.2.4 Add Raw Materials identified as Prohibited Risk to form D-302-F2 Prohibited Risk Raw Material List.

8.2.5 Sign the form.

8.2.6 When new raw materials are added to the Prohibited list, DC will replace previously approved D-302-F2 Prohibited Risk Raw Material List forms with the most current form and will publish the form for reference by QC lab Management.

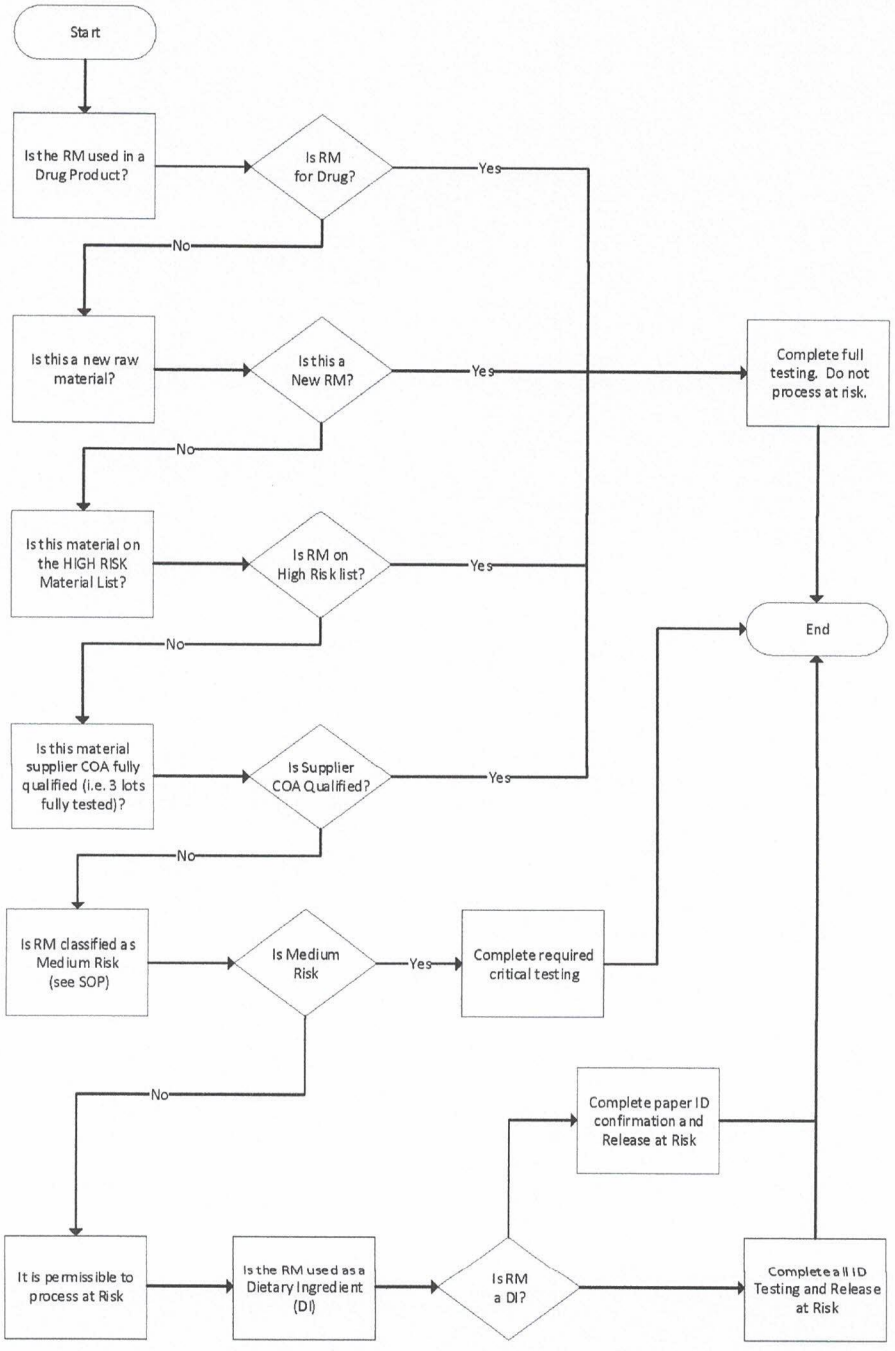
9.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	10/06/22	New procedure.	N/A	J. Sassman
1	03/12/24	Edited F1 for the following: Changed override requirements to operations management to quality management, added N/A check boxes where applicable, eliminated signature requirements at the bottom of the first page.	CC-24-0093	A. Shannon

10.0 Attachments

10.1 Attachment 1 – Flow Chart for At Risk Use Determination

Attachment 1 – Flow Chart for At Risk Use Determination



RM Description	
RMID	
R #	

PHASE 1

Decision Questions

Start with Question 1. Proceed to additional questions as directed by each answer until the answer identifies a path forward. Once a path forward has been identified, select N/A for all questions not executed.

Question	Answer
Q1 – Is RM for drug? Is the RM used in a Drug Product?	☐ Yes – Complete full testing. Do not release at risk. Do not complete additional questions ☐ No – Go to Q2
Q2 – Is this a new RM? Is this a new raw material?	☐ Yes – Complete full testing. Do not release at risk. Do not complete additional questions ☐ No – Go to Q3 ☐ N/A
Q3 – Is RM on Prohibited/ High Risk List? Is the raw material on the prohibited risk material list or Is this raw material classified as High Risk?	☐ Yes – Complete required critical testing (define below). Do not release at risk until required testing is successfully completed. Do not complete additional questions ☐ No – Go to Q4 ☐ N/A
Q4 – Is this material supplier COA Qualified? Is this material supplier COA fully qualified (i.e. 3 lots fully tested)?	☐ No – Complete full testing. Do not release at risk. Do not complete additional questions ☐ Yes – Go to Q5 ☐ N/A
Q5 – Is RM Medium Risk? Is the raw material classified as Medium Risk? All other raw materials will default to classification Low Risk.	☐ Yes – Complete required critical testing (define below). Release at risk after required testing is successfully completed. ☐ No – Complete paper ID confirmation (C of A review). Release at risk ☐ N/A

Required Testing to release material at risk:

Decision Questions

Transfer the result from the above questions to one of the options below (select only one).

- ☐ Complete full testing. Do not release at risk
- ☐ Complete required testing. Do not release at risk until testing completed.
- ☐ Complete paper ID confirmation. Release at risk.
- ☐ Release at risk override with Operations and Quality Management Approval (signatures required below).

Release at Risk Override Approvals or ☐ N/A

Name	Title	Signature	Date
Operations Mgmt:			
Quality Mgmt:			

Phase 1 evaluation completed by:

Name	Title	Signature	Date

PHASE 2 – Completion

- ☐ No testing required, COA reviewed. Raw material approved to be used at risk.
- ☐ Required testing successfully completed on _____. Raw material approved to be used at risk.
  (date)
- ☐ Required testing not successful. Raw material cannot be used at risk.
- ☐ N/A (Override approved)

Name	Title	Signature	Date
Completed By: (Author)			
Approved By: (DC)			