ION LABS QUALITY FIRST	Standard Operating Procedure **Standardized Botanical Raw Materials**	**SOP Number** **D-301**	**Revision** **1**
		Effective Date 05/14/19	**Page** **Page 1 of 3**
Written by/ Date 04/15/19	**Reviewed by/ Date** JG 04-17-19	**Approved by/ Date** SSR 04/17/19	
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1.0 Purpose

The purpose of this SOP is to define guidelines for setting limits on allowable variation of standardized chemicals in botanical extracts.

2.0 Scope

This SOP applies to all standardized botanical extracts with single or multi-chemical component standardizations. The guidelines also apply to digests of botanical subcomponents. These guidelines do not apply to fine chemicals or whole botanicals. These guidelines do not apply to quantitation of trace toxins or chemicals that only have an upper limit.

3.0 Responsibility

3.1 It is the responsibility of QC Laboratory Chemists to follow these guidelines for raw material release.

3.2 It is the responsibility of R&D to formulate for label claims using these guidelines.

3.3 It is the responsibility of QC Laboratory Management and R&D to set acceptable variability for a standardized botanical extract and to ensure this procedure is being followed.

3.4 It is the responsibility of the QC Laboratory Management to keep SOP up to date with current practices.

4.0 Definitions

4.1 **USP** – United States Pharmacopeia

4.2 **QC** – Quality Control

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

4.4 **RMTT** – Raw Material Test Ticket

4.5 **CofA** – Certificate of Analysis

4.6 **HPLC** – High Performance Liquid Chromatography

4.7 **RSD** – Relative Standard Deviation

5.0 References

None

6.0 Procedure

6.1 General Guidelines

6.1.1 When an allowed variation is set for the strength metric of a standardized botanical extract the activity factor listed in the raw material database will be adjusted to the maximum allowed variation for raw material release.

Example: Strength standardized to 50% Component A

Allowed variability= +/- 10% or 0.1

Activity = 1 – 0.1 = 0.9

6.1.2 When R&D is formulating for a strength label claim for a standardized botanical extract the adjusted activity factor will be used.

6.1.3 When R&D is formulating with a standardized botanical extract and no label claim is made the activity factor used in the formulation is 1.

6.1.4 For QC Laboratory raw material release, the specified variation of a standardized material will be listed on the RMTT for the material. The allowed variability will be in the format: Strength claim +/- X%.

6.1.5 The QC laboratory can calculate the acceptable upper and lower thresholds as follows:

Example: Strength standardized to 50% Component A

Allowed variability- +/- 10%

Low threshold of activity = 0.5 * (1 – 0.1) = 0.45 = 45%

Upper threshold of activity = 0.5 * (1 + 0.1) = 0.55 = 55%

6.1.5.1 Being within the upper threshold is not a requirement for raw material release unless an upper limit is specified by the raw material

manufacturer or requested by the customer. The upper limit cannot exceed 100% purity + the %RSD of the assay.

6.2 Single Chemical Standardization

6.2.1 For single chemical strength claims in a botanical extract the maximum variability allowed is 20% for claims ≤ 5% and 10% for claims > 5%.

6.2.2 Maximum variability allowed when the raw material is standardized by the manufacturer using titration and the CofA challenge determination using HPLC is 25% for claims ≤ 5%, 15% for claims > 5% but < 50%, and 10% for claims ≥ 50%. This should be used as a rule of thumb. Raw materials may be more potent from the vendor and should be examined to determine if the values listed above are appropriate.

6.2.3 Deviations from these variations are permitted with documented justification.

6.3 Multi-chemical / Chemical Class Standardization

6.3.1 For multiple-chemical strength claims in a botanical extract that use separate standards the maximum variability allowed is for each determination is 20% for claims ≤ 5% and 10% for claims > 5%.

6.3.2 For strength claims that apply to a class of chemicals (i.e. alkaloids, polyphenols, etc.) and the quantitation is a summation of individual chemicals using a single chemical reference standard, the maximum variability allowed is 25% for claims ≤ 5% and 15% for claims > 5%. This should be used as a rule of thumb. Raw materials may be more potent from the vendor and should be examined to determine if the values listed above are appropriate.

7.4 The allowed ranges for single and multi-chemical standardizations are the maximum recommended ranges to use without justification. Many factors may be considered in selecting a range of variability, including quality of the standards, type of assay used, and impact assessment on fill weight or tablet weight.

7.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	08/03/15	New	15-0695	B. Johns
1	04/08/19	Scheduled review: Added explanations to the standardization specs	19-0237	J. Maignan