

	Standard Operating Procedure Calculations for Ingredient Addition Verification for Finished Products		SOP Number D-403	Revision 6
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Written by/ Date <i>Shirley 08/15/24</i>		Reviewed by/ Date <i>[Signature] 08/20/24</i>		Approved by/ Date <i>[Signature] 08/20/24</i>
Title: Director of Quality Control		Title: Director of Product Development		Title: Director of Quality Assurance

1.0 Purpose

This procedure describes the process used to calculate the results for the Ingredient Addition Verification in order to verify the amount of an ingredient declared on the product label which does not have a scientifically valid test method available to analyze.

2.0 Scope

This procedure applies to all raw materials used in dietary supplements, foods, and pet supplements that have declared label claims for which a valid analytical method is unavailable.

3.0 Responsibility

- 3.1 It is the responsibility of R&D and QC to determine IAV requirements when drafting a new product's Product Profile, and to include these requirements in the finished product testing section of the profile.
- 3.2 It is the responsibility of R&D to review and approve a product's IAV template created by Document Control.
- 3.3 It is the responsibility of Document Control to create IAV forms when creating new master batch records, as required by the product's Product Profile. Document Control is also responsible for ensuring that approved IAV forms are included as part of the executed batch record for each product that requires IAV to be performed.
- 3.4 It is the responsibility of the QC Laboratory to perform the calculations necessary to verify the correct addition of each required ingredient to the batch, and to complete the

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IAV with the results of these calculations. It is also the responsibility of the QC Laboratory to check these results and initial and date each value entered, as well as sign and date the completed IAV and calculation sheet.

- 3.5 It is the responsibility of Quality to review, verify, and approve the IAV values and calculations, and to sign and date the IAV form.

4.0 Definitions

- 4.1 **IAV** – Ingredient Addition Verification
- 4.2 **DC** – Document Control
- 4.3 **R&D** – Research and Development
- 4.4 **BPR** – Batch Production Record
- 4.5 **COA** – Certificate of Analysis
- 4.6 **QC** – Quality Control
- 4.7 **NLT** – Not Less Than

5.0 References

- 5.1 D-401, SOP, New Product Documentation Requirements
- 5.2 C-201, SOP, Deviation and Investigation Procedure
- 5.3 C-502, SOP, Record Storage, Retention, and Destruction
- 5.4 21 CFR 111.75 - What must you do to determine whether specifications are met?
- 5.5 21 CFR 111 subpart M – Holding and Distributing

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6.0 Procedure

6.1 Products manufactured in-house at Ion Nutritional Labs facilities will be qualified by verifying that using a specific set of raw materials evaluated in accordance to the Raw Material Testing Summary, warehouse controls, a master formula, master batch record, manufacturing controls, and quality management systems to ensure that the dietary supplement product consistently meets the established product specifications. The warehouse controls are set in place to comply with warehouse or other storage facilities holding a dietary supplement as described in subpart M in FDA 21 CFR 111. The requirements for release are that every finished batch of dietary supplement meets each product specification for identity, purity, strength, composition and limits on contamination that may adulterate a finished product produced at Ion Nutritional Labs as per 21 CFR 111.75.

6.2 Calculating Results for the IAV

6.2.1 Dosage Weight

6.2.1.1 Tablets

- The average weight per tablet in grams is calculated from a composite of NLT 20 tablets. The average weight calculated from the QC Laboratory weight variation assessment or a composite analysis from the tablet run record can be used.

6.2.1.2 Capsules

- The average fill weight per capsule in grams is calculated from a composite of NLT 20 capsules. The average fill weight calculated from the QC Laboratory weight variation assessment minus the weight of the empty capsule or a composition analysis of the

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capsule run record minus the weight of the empty capsule can be used.

6.2.1.3 Powders and Liquids

- The powder and liquid weights in grams are determined by the serving size from the BPR.

6.2.1.4 Gummies

- The gummy dosage weight is taken from the average of the deposit weights as recorded in the Batch Record.

6.2.2 Total Batch Weight

6.2.2.1 Tablets, Capsules, Powders, and Liquids

- The total batch weight is obtained from the weigh and mix order.

6.2.2.2 Gummies

- Given the nature of gummy manufacturing which involves both continuous and batch processes, as well as removing significant quantities of water from the formula, the total batch weight is not used in calculations. However the total batch weight of an individual active sub-blend is calculated by reviewing the batch record. The acid and flavor (added after the sub-blend) is incorporated in this weight by multiplying the sub-blend weight by the ratio of combined flow rates to base flow rate.

6.2.2.3 Dosage Units per batch

- The total number of dosage units in a batch of tablets, capsules, powder servings, and liquid servings is calculated by taking the

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total batch weight in kilograms, converting to grams, and dividing by the average dosage weight in grams.

- Dosage units per batch are not considered for gummies

6.2.3 Ingredient Weight per Dose

6.2.3.1 If a raw material with a label claim does not have a validated test method due to selectivity, sensitivity, sample extraction efficiency or other limitation or requirement, IAV can be performed.

Example 1: Vitamin B12 as Methylcobalamin, using the weigh and mix, the actual input of Vitamin B12 is divided by the actual batch weight then multiplied by 100 to get the percent composition of Vitamin B12 in the dose. The %composition of Vitamin B12 is multiplied by the average tablet weight in milligrams then multiplied again by the % chemical activity (purity) obtained from the manufacturer or internal CofA on the as-is basis to get the mg Vitamin B12 in the dose.

Example 2: In the case of calcium in calcium carbonate, the calculation would be similar to Example 1 with the difference of the weight of the calcium carbonate would be adjusted for purity then multiplied by 0.4 (40%) to calculate the calcium content (Calcium MW = 40, Carbonate MW = 60).

Example 3: In the case of methylcobalamin in a gummy formulation. The amount of methylcobalamin added to one sub-blend would be divided by the total sub-blend weight (including acid and flavor) for a % by weight

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value. That % is then multiplied by the deposit weight, then multiplied again by the % chemical activity (purity) obtained from the manufacturer or internal CofA on the as-is basis to get the mg Vitamin B12 in the dose.

6.2.3.2 If the serving size is more than one, multiply the amount of the ingredient per dosage unit by the serving size to determine the ingredient weight per serving.

6.2.4 Proprietary Blends

6.2.4.1 Proprietary blends are quantified based on the batch record, the inputs of which are verified through the weigh and mix. IAV is not required.

6.2.4.2 If an assayable analyte is present in a proprietary blend, the analyte will require testing if a scientifically valid test method is available.

6.2.4.3 Customer requirements supersede any internal IAV requirements.

6.2.5 Calculation Record

6.2.5.1 A record is prepared for all calculations and results for each raw material requiring IAV (refer to Attachment 1 – IAV Record and Calculations Example). The completed record is attached to the IAV in the BPR.

6.2.5.2 If an Excel spreadsheet is used to calculate IAV and the spreadsheet is not locked and validated, a sample calculation must be performed in a laboratory notebook to verify the spreadsheet calculation, reviewed, and submitted with the approved IAV record.

6.3 Completion of the IAV

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6.3.1 Entering Results

6.3.1.1 The batch weight of each ingredient requiring IAV is entered in the appropriate location on the IAV spreadsheet. The calculated amount of each ingredient is compared to the label claim for that particular ingredient or blend, and must be not less than 100% of the label claim (or customer requested range if applicable) from the approved product label or supplement facts.

6.3.2 Verify and Sign

6.3.2.1 Each entry is verified. One result in each IAV is verified by manual calculation to verify the spreadsheet equation if the spreadsheet isn't validated. The ingredient units are checked against the units listed on the IAV. Each entry is initialed and dated. The form and the calculation record are signed and dated.

6.3.3 Final Verification

6.3.3.1 The completed IAV and the substantiating calculation record are reviewed, verified, and approved as part of the completed finished product test packet by the QC Laboratory.

6.3.4 If IAV results fall outside of the specified acceptance range, a deviation investigation should be initiated. Refer to SOP C-201 Deviation and Investigation Procedure.

6.3.5 Completed IAV forms are submitted to Document Control as part of the finished product release packet. Release documents are filed with the executed batch records and maintained as per SOP C-502 Record Storage, Retention, and Destruction.

7.0 Revision History

Revision	Date	Description of Changes	CCR #	By
1	05/31/13	New procedure.	13-330	G. Lanke
2	06/16/15	Added note for IAV as needed for liquid products.	15-0519	J. Cobos
3	08/27/17	Add clarification to which ingredients will utilize the IAV method.	17-0913	L. Titolo
4	07/10/18	Clarified language surrounding requirements of 21 CFR 111.	18-0232	J. Coyle
5	01/12/22	Updated to reflect current practices.	CC-22-0017	J. Sassman
6	08/01/24	Clarified calculations for IAV. Clarified sources of input for IAV calculations. Redefined the calculation process for proprietary blends. Expanded requirements for IAV calculations and reporting.	CC-24-0319	B. Johns

8.0 Attachments

- 8.1 Attachment 1 – IAV Calculations Example
- 8.2 Attachment 2 – IAV Specification and Results Form Example

Attachment 1 – IAV Calculations Example

Ingredient Addition Verification Specification and Results Record and Calculations Example							
Results Formulas for Each Ingredient*:		Ion Labs <i>Garcinia cambogia</i> Capsules Batch # XXXXXX				SMPXXXXP1Q150	
Average weight of each capsule from Encapsulation Run Record: 0.7560 g/capsule							
Average fill weight of each capsule equals: 0.7560 g/capsule - capsule weight of a "00" Capsule 0.120 g = 0.6360 g/capsule.							
Total capsule fill gross weight from weight and mix yield: 572.4 kg/batch							
Total capsules produced in 572.4 kg/batch X 1000 g/kg = 572,400 g/batch / 0.636 g/cap = 900,000 capsules/batch							
Ingredient 1: Calcium (As Calcium Carbonate) 37.0 Percent Calcium							
Actual weight ingredient used in the batch: 60.81 kg X percent active 37.0 % = Weight of Calcium 22.4997 kg/batch							
Weight of Calcium per batch: 22.4997 kg/ Number of capsules: 900,000 = Weight per capsule: 0.00024999667 kg							
Weight Calcium per capsule: 0.00024999667 Kg X 1,000,000 mg/kg = the weight of 25.00 mg Calcium in each Capsule.							
25.00 mg Calcium in each Capsule X 2 capsules per serving = 50.00 mg Calcium per serving.							
Ingredient 2: Potassium (as Potassium Chloride) 52.4 Percent Potassium							
Actual weight ingredient used in the batch: 42.94 kg X percent active 52.4 % = Weight of Potassium 22.50056 kg/batch							
Weight of Potassium per batch: 22.50056 kg/ Number of capsules: 900,000 = Weight per capsule: 0.00025000622 kg							
Weight Potassium per capsule: 0.00025000622 Kg X 1,000,000 mg/kg = the weight of 25.00 mg Potassium in each Capsule.							
25.00 mg Potassium in each Capsule X 2 capsules per serving = 50.00 mg Potassium per serving.							
Ingredient 3: Chromium (as Chromium Amino Acid Chelate) 10.0 Percent Chromium							
Actual weight ingredient used in the batch: 0.9 kg X percent active 10.0 % = Weight of Chromium 0.09 kg/batch							
Weight of Chromium per batch: 0.09 kg/ Number of capsules: 900,000 = Weight per capsule: 0.00000100000 kg							
Weight Chromium per capsule: 0.00000100000 Kg X 1,000,000 mcg/kg = the weight of 100.00 mcg Chromium in each Capsule.							
100.00 mcg Chromium in each Capsule X 2 capsules per serving = 200.00 mcg Chromium per serving.							
Ingredient 4: Garcinia cambogia Extract 4:1 100.0 Percent Garcinia cambogia Extract							
Actual weight ingredient used in the batch: 450 kg X percent active 100 % = Weight of Garcinia cambogia Extract 450 kg/batch							
Weight of Garcinia cambogia Extract per batch: 450 kg/ Number of capsules: 900,000 = Weight per capsule: 0.000500000000 kg							
Weight Garcinia cambogia Extract per capsule: 0.000500000000 Kg X 1,000,000 mg/kg = the weight of 500.00 mg Garcinia cambogia Extract in each Capsule.							
500.00 mg Garcinia cambogia Extract in each Capsule X 2 capsules per serving = 1000.00 mg Garcinia cambogia Extract per serving.							
Generated By / Date				Reviewed By / Date			
*All calculations generated manually.							

Attachment 2 – Ingredient Addition Verification Specification and Results Form Example

Ingredient Addition Verification Specification and Results Form (Example)

Customer Name: Ion Labs
 Product Name: Garcinia Cambogia Capsules SMP0000P1Q1S0

Ingredient Name	Label Claim (LC)	Minimum Specification (95% of LC)	Maximum Specification (105% of LC)	Results	Calculated By/Date
Calcium (as Calcium Carbonate)	50.0000 mg	47.5000 mg	52.5000 mg		
Potassium (as Potassium Chloride)	50.0000 mg	47.5000 mg	52.5000 mg		
Chromium (as Chromium Amino Acid Chelate)	200.0000 mcg	190.0000 mcg	210.0000 mcg		
Garcinia cambogia Extract	1,000.0000 mg	950.0000 mg	1,050.0000 mg		

(Y/N) Ingredient name(s) and label claim(s) match proposed label (or supplement facts if label is not available)
 (Y/N) Specification calculations have been verified

Reference: _____
 Comments: _____

Generated By DC/Date: _____ Reviewed By Quality/Date: _____

Refer to last page for all Results Calculation Formulas.

(Y/N) Ingredient name(s) and label claim(s) match approved label.
 Reviewed By Quality/ Date: _____

Note: If any changes have occurred, a new Ingredient Addition Verification Specification and Results Form will be generated and approved prior to the calculation of results

(Y/N) Results formulas and calculations have been verified
 (Y/N) All results are within specification
 Comments: _____

Performed By R&D /Date: _____ Approved By Quality/Date: _____