1.0 Purpose

The purpose of this procedure is to outline the numerical conversions required to the convert units of concentration for strength test results into the units required for evaluation of product label claims. Additionally, this procedure may assist in the development of new products to ensure that the product formulation contains an appropriate quantity of raw material to meet the label claim. This procedure helps to ensure compliance with regulatory requirements and consistency in labelling of dietary supplements.

2.0 Scope

This procedure applies to the determination of vitamins including A, B1, B2, B3, B5, B6, B7, B9, B12, C, D, and E in the QC laboratory at Ion Labs. This procedure applies to the formulation of new products in the R&D laboratory at Ion Labs.

3.0 Responsibility

3.1 It is the responsibility of QC Chemists and R&D formulators to follow this procedure.

3.2 It is the responsibility of QC Laboratory Management and R&D Management to implement this procedure and to ensure that the procedure is being followed.

3.3 It is the responsibility of QC Laboratory Management and/or Analytical Development to keep the procedure current with Ion Labs practices.

4.0 Definitions

4.1 **QC** – Quality Control

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

4.3 **NLT** – No Less Than

4.4 **DFE** – Dietary Folate Equivalents

4.5 **RAE** – Retinol Activity Equivalents

4.6 **FP** – Finished Product

4.7 **Vitamin A** – A lipid soluble group of related organic compounds with a long carbon chain consisting of at least four conjugated double bonds often terminating in a ring. The vitamin A content of dietary supplements is expressed on the label as retinol activity equivalents (RAE).

4.8 **Vitamin B1** – Thiamine (also called thiamin, a water soluble vitamin).

4.9 **Vitamin B2** – Riboflavin and riboflavin-5-phosphate (a water soluble vitamin).

4.10 **Vitamin B3** – Niacin (also called nicotinic acid, a water soluble vitamin). Niacinamide is another form of Vitamin B3 with identical vitamin activity to niacin. The amino acid tryptophan is a precursor for niacin synthesis, and therefore, can also be used to supply Vitamin B3 in dietary supplements.

4.11 **Vitamin B5** – Pantothenic acid (a water soluble vitamin). Vitamin B5 is most commonly supplied as calcium-D-pantothenate in dietary supplements as the calcium salt is more stable than pantothenic acid and easier to work with.

4.12 **Vitamin B6** – A group of chemically similar water soluble compounds which can be interconverted in biological systems. Often supplied in the form of pyridoxine hydrochloride or pyridoxal-5-phosphate in dietary supplements.

4.13 **Vitamin B7** – Biotin (a water soluble vitamin).

4.14 **Vitamin B9** – A water soluble vitamin with multiple forms which are collectively referred to as folate. Most often supplied as folic acid or methyltetrahydrofolate in dietary

supplements. The vitamin B9 content of dietary supplements is expressed on the product label as dietary folate equivalents (DFE).

4.15 **Vitamin B12** – A class of water soluble vitamins referred to as cobalamins. Common forms in dietary supplements include methylcobalamin and cyanocobalamin.

4.16 **Vitamin C** – Ascorbic acid (a water soluble vitamin and antioxidant).

4.17 **Vitamin D** – A group of lipid soluble secosteroids. Commonly supplied as cholecalciferol or ergocalciferol in dietary supplements.

4.18 **Vitamin E** – A group of lipid soluble compounds that includes tocopherols and tocotrienols. Often supplied as esterified forms (tocopherol acetate or tocopherol succinate) in dietary supplements due to their decreased susceptibility to oxidation relative to tocopherol.

4.19 **Vitamin K** – A group of related lipid soluble compounds which differ in the number of double bonds and length of the side chain. Two common forms in dietary supplements are menaquinone-4 (MK-4) and menaquinone-7 (MK-7).

5.0 References

5.1 Code of Federal Regulations, 21CFR 109.9 (c) (8) (iv)

5.2 US Food and Drug Administration, *Converting Units of Measure for Folate, Niacin, and Vitamins A, D, and E on the Nutrition and Supplement Facts Labels: Guidance for Industry*, August 2019.

5.3 National Institutes of Health – Office Of Dietary Supplements, https://dsid.od.nih.gov/conversions.php (accessed 12/07/22), Dietary Supplement Ingredient Database – Unit Conversions

6.0 Conversion Factors in Analytical Determinations

6.1 Determine the label claim of the product being tested (Table 1 - first column).

6.2 Determine the raw material used to supply the label claim in the finished product (Table 1 - second column).

6.3 Perform the analytical determination.

6.3.1 In general, the reference standard used should be the same chemical form as the raw material used in the finished product.

6.3.2 Thiamine HCl and thiamine mononitrate reference standards may be used interchangeably.

6.3.3 Pyridoxine and pyridoxine HCl reference standards may be used interchangeably.

6.4 Determine the conversion factor (Table 1 - third column).

6.4.1 In the case of an analytical determination for Vitamin B1 or B6 where the reference standard is not the same chemical form as the raw material used in the finished product, use the conversion factor in Table 1 that corresponds to the reference standard used (not the raw material used in the finished product).

6.5 Multiply the result of the analytical determination by the conversion factor. This is often performed within the chromatographic software by using a multiplier.

6.6 Example 1: The product contains pyridoxine HCl with a label claim of 0.5 mg vitamin B6. Strength testing is performed by HPLC using pyridoxine HCl reference standard, and the result is 0.7 mg per dosage unit. The conversion factor for pyridoxine HCl is 0.823. Therefore, the amount of vitamin B6 in the product is 0.7 mg × 0.823 = 0.576 mg or 115% of label claim.

6.7 Example 2: The product contains thiamine mononitrate with a label claim of 1.5 mg of vitamin B1. Strength testing is performed using thiamine hydrochloride reference standard, and the result is 2.3 mg per dosage unit. The conversion factor for thiamine HCl

is 0.787. Therefore, the amount of vitamin B1 in the product is 2.3 mg × 0.787 = 1.81 mg or 121% of label claim.

7.0 Conversion Factors in Product Formulation

7.1 Determine the label claim of the product being tested (Table 1 - first column).

7.2 Determine the raw material used to supply the label claim in the finished product (Table 1 - second column).

7.3 Determine the conversion factor for the raw material (Table 1 – third column).

7.4 Determine the purity of the raw material from the raw material manufacturers certificate of analysis or by estimation if a source for the raw material has not yet been identified.

7.5 Determine the desired overage for the raw material.

7.6 Determine the amount of raw material required to be added to the product.

7.6.1 Divide the label claim by the purity factor in decimal format.

7.6.2 Multiply the result of 7.7.1 by the overage in decimal format.

7.6.3 Divide the result of 7.7.2 by the conversion factor.

7.7 Example 3: The product has a label claim of 0.6 mg Vitamin A. Retinyl palmitate with a purity of NLT 7.5% will be used to supply Vitamin A in the finished product with an overage of 40%. The amount of raw material needed for the formulation is 0.6 mg ÷ 0.075 × 1.4 ÷ 0.546 = 20.5 mg.

Table 1: Conversion Factors for Evaluating Label Claims and New Product Formulation

Label Claim	Raw Material used in FP	Conversion Factor
Vitamin A (RAE)	Retinol	1
	Retinyl Acetate	0.872
	Retinyl Palmitate	0.546
	β-Carotene	0.5
Vitamin B1	Thiamine HCl	0.787
	Thiamine Mononitrate	0.811
Vitamin B2	Riboflavin	1
	Riboflavin-5-Phosphate	1
Vitamin B3	Nicotinic Acid	1
	Niacinamide	1
	Tryptophan	0.0167
	Niacinamide Ascorbate	*
	Inositol Nicotinate	0.911
Vitamin B5	Calcium-D-Pantothenate	0.920
Vitamin B6	Pyridoxine	1
	Pyridoxine HCl	0.823
	Pyridoxal-5-Phosphate	1
Vitamin B7	Biotin	1
Vitamin B9 (DFE)	Folic Acid	1.7
	Calcium-DL-5-Methyltetrahydrofolate	1.7
	Calcium-L-5-Methyltetrahydrofolate	1.7
	L-5-Methyltetrahydrofolate	1.7
Vitamin B12	Cyanocobalamin	1
	Methylcobalamin	1
Vitamin C	Ascorbic Acid	1
	Ascorbyl Palmitate	0.425
	Niacinamide Ascorbate	*
Vitamin D	Cholecalciferol	1
	Ergocalciferol	1
Vitamin E	D-α-Tocopherol (RRR-α-Tocopherol)	1
	DL-α-Tocopherol	0.5
	DL-α-Tocopherol Acetate	0.5
	D-α-Tocopheol Acetate	1
	DL-α-Tocopherol Succinate	0.5
	D-α-Tocopherol Succinate	1
Vitamin K	Vitamin K1 (phylloquinone)	1
	Vitamin K2 (menaquinone)	1
	Vitamin MK-4 (menaquinone-4)	1
	Vitamin MK-7 (menaquinone-7)	1

* For formulating finished product: consult raw material CoA for vitamin B3/C content; for analytical testing: use multiplier of 1 with either niacinamide or ascorbic acid standard

8.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	12/20/22	New procedure.	N/A	S. Sassman
1	01/17/24	Add conversion factors for additional vitamers.	CC-24-0024	S. Sassman
2	05/06/24	Add conversion factor for ascorbyl palmitate	CC-24-0188	S. Sassman