REPUBLIC OF RWANDA

RWANDA FDA
Rwanda Food and Drugs Authority

GUIDELINE FOR EVALUATION OF FOOD SUPPLEMENT

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FOREWORD

The Rwanda Food and Drugs Authority (RWANDA FDA) is a regulatory body established by the Law N° 003/2018 of 09/02/2018. One of the functions stated in this Law is to regulate matters related to quality and safety of food for the purpose of protecting the public from health hazards associated with the consumption of food, especially in its article 3(3) and 8(8).

Food supplements effects is one of the public health concerns not only to our country but all over the world. It is in this context that the Rwanda Food and Drugs Authority intends to put in place guidelines that provides an approach for evaluation of food supplements to ensure that they do not constitute harmful effects to people's health and leads to losses of life.

It is expected that these guidelines will offer a clear understanding to evaluators ,manufacturers to be evaluated and other persons concerned by the guidelines during the evaluation process, they will protect consumers from and food manufacturing industry,thus promoting health protection,business and the national economy as a whole.

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DIRECTOR GENERAL
RWANDA FOOD AND DRUGS AUTHORITY

ABBREVIATIONS

EFSA	European Food Safety Authority
FAO	Food and Agriculture Organization
FDA	Food and Drugs Authority
GMP	Good Manufacturing Practices
HACCP	Hazard Analysis Critical Control Point
RDA	Recommended Daily Allowance
RDI	Recommended Daily Intake
Rwanda FDA	Rwanda Food and Drugs Authority
USL	Upper Safe Level
WHO	World Health Organization

CHAPTER 1
INTRODUCTION AND DEFINITIONS OF TERMS

1.0 INTRODUCTION

Assessment of applications for registration of food supplement is an important aspectof effective control of quality and safety of such products in order to ensure that those recommended for registration meets set standards/requirements.

This document is intended to guide evaluators of Food Supplement to effectively assess the quality and safety of such foods in order to ensure that those recommended for registration meet acceptable requirements.

Food Supplements are normally used because of their specific nutritional demand, for instance, as sources of vitamins, minerals, amino acids or fatty acids, in order to supplement the diet. They may also have a physiological effect in the body of the intended user for instance on digestion, blood pressure or cholesterol level.Rapid increase in consumption of Food Supplements and demand of diversified varieties enhanced market promotion compelled the adoption of appropriate control measures to protect consumer health.

These guidelines prescribe general and specific requirements that assist the evaluator to assess application documents and samples submitted for registration.

It is expected that these Guidelines will help evaluators to efficiently and effectively assess the safety and quality, including information and claims of such products aiming at ensuring that those Food Supplements recommended for registration are safe for human consumption.

1.1 DEFINITION OF TERMS

a) **Adequate Intake (AI):** The recommended intake based on experimental or observed approximations of nutrient intake by groups of healthy individuals, which are assumed adequate. These are used when RDA's can't be determined.

b) **An ingredient** means a substance or product, including additives, that has been used in the manufacture of a food product and that remains in the final food product in some form.

c) **Authority** Means Rwanda Food and Drugs Authority.

d) **Certificate of GMP or HACCP Compliance** Means a certificate or warranty accompanying an application for registration of food supplements to be imported into

thecountry issued by competent authority certifying that the manufacturing premises comply with GMP or HACCP.

e) **Characteristicingredient/**substance in a food supplement means a nutrient such as vitamins or minerals or some other substance with a nutritional or physiological effect. Nutrients may also include e.g. fibre, amino acids, and edible fats, fatty acids vitamins, carbohydrates, plant extracts, herbs, bee products, microbes, bone meal, dolomite, ashes, horn powder, enzymes, colostrum and organic matter.

f) **Codex** Means the Codex Alimentarius Commission responsible for execution of the joint FAO/WHO food standards programme for the purpose of protecting the health of food consumers and ensuring fair practices in the international food trade.

g) **Diet** means the sum of food consumed by a person.

h) **Food Additive** Means any substance, other than a typical ingredient, which has been appropriately evaluated for safety and quality and is included in a food supplement for a specific reason (e.g. to maintain stability of the finished product).

i) **Food** Means any article other than drugs, cosmetics and tobacco used as food or drink for human consumption and includes any substance used inthe manufacture or treatment of food.

j) **Food/dietary supplement**Means a product other than tobacco intended to supplement nutrients in the diet, and contains concentrated source of one or a combination of the following:

i) Vitamins;
ii) Minerals;
iii) Amino acids;
iv) Essential fatty acids;
v) Enzymes and other Metabolites;
vi) Pre and/or probiotic;
vii) Natural substances of plant or animal origin with nutritional or physiological function;

Intends to be taken orally in the form of tablet, capsule, powder, soft gel, gel cap, pellet, pill, granules or liquid; It is not presented for use as a convectional food or as a substitute of a meal or the diet; Labelled and marketed as food/dietary supplement and does not suggest in any way that the product is meant to diagnose, treat, cure or prevent a disease, disorder, abnormal physical or mental state or a particular physiological function.

k) **Nutrient** means any substance normally consumed as a constituent of food which provides energy or which is needed for growth, development and maintenance of life; or a deficit of which will cause characteristic bio-chemical or physiological changes to occur.

l) **Physiological function** means functions carried out by organs, tissues and cells to maintain the body in good health or to keep the body in a state of homeostasis;

m) **Recommended Nutrient Intake** or **Reference Daily Intake (RDI)** or **Recommended Dietary Allowance (RDA)** means the average level of daily dietary intake which is sufficient enough to meet nutrient requirements of 97– 98 percent of healthy persons in particular life stages and gender groups.

n) **Special Diet products** means food products that are different from corresponding ordinary food in composition or manufacturing for vulnerable group;

o) **Upper Safe Levels (USL)** means the highest level of nutrient intake that is likely to pose no risk of adverse health effects for almost all individuals in the general population. As intake increases above the USL, the risk of adverse effects increases.

CHAPTER 2

2.0 GENERAL REQUIREMENTS FOR EVALUATION OF DIETARY SUPPLEMENTS

2.1 Application Documents and Samples

Application for registration of food supplement shall include the following documents:-

a) Application documentssuch as application forms,manufacturing process flow diagram copy of certificate of GMP or health certificate issued by competent Authorities from the country of origin, ISO or HACCP compliance certificate, certificates of analysis, stability study report, and quality and safety data.

b) Five (5) unitsof commercial labelled samples.

2.2 Mobilisation of Evaluation Tools

The evaluator has to gather the following tools for use during evaluation of dietary supplements;

a) Guidelines for evaluation of dietary supplements;

b) Guidelines for application for registration of prepackaged foods in Rwanda;

c) Registration of Food Regulations;

d) Food Labelling Regulations;

e) Relevant National and/or Codex standard and/or Internationally recognized standards Including pharmacopeia;

f) Relevant sources of information such as WHO/FAO, EFSA, FDA published guidelines and technical reports;

g) The National standards of permissible food additives and their levels of use and/or Codex General Standard for Food Additives;

h) CODEX Guidelines for use of Nutrition and Health claims;

2.3 Evaluationof Documents and Samples

At this stage, evaluation is done to ascertain compliance of application to quality and safety requirements based on the tools outlined in clause 2.2 above. During evaluation, observations, comments and shortcomings shall be recorded in the appropriate evaluation report for food supplements. The evaluator shall conduct critical evaluation of documents and samples as follows:-

2.3.1 **Particulars of the sample**

a) **Brand name**

i) Examine the brand name declared in the application form to ascertain if it isthe same as the one appearing on the product sample.

ii) Examine to ascertain if the brand name is neither misleading nor confusing to the consumer and not suggestive of any other product with which such a product might be confused.

b) **Common name**

i) Examine the common name declared in the application form to ascertain it is thesame as the one appearing on the product sample.

ii) Examine the common name on the application form to ensure that it accurately describes the nature of the product.The name of the product shall be "food supplement" or 'Dietary supplement' with an indication of the category of nutrients or of the individual vitamin(s), mineral(s), amino acids, essential fatty acids, specific substance(s) of plant or animal origin, enzymes or any combination of any of these ingredients contained in the product.

c) **Product form**

Examine product dosage form (i.e. Tablets, capsules, soft gels,solid, liquid, powder and suspension) appearing on the application form and sample to verify its accuracy in describing the product as evidenced by the sample.

d) **Intended use of the product**

Examine the intended use of the product declared in the application form to ascertain samenesswith information on the label. Also examine if the product is intended for supplementation.

e) **Concentration and dosage of characteristic ingredients**

Examine the dose recommended by manufacturer with respect to user age group and physiological condition to ensure that:

i) The levels are not below the minimum requirements for each ingredient intended for supplementation and;

ii) The levels of each ingredient do not exceed the safe limit.

f) **Packaging material**

Examine the packaging materials; both primary and secondary (if any) to ascertain that they are of acceptable types and qualities and safeguard the quality and hygienic properties of the product.

g) **Closure and seal**

Examine the cap, crown, lid, blister or closure to establish that it is of acceptable type and quality. Examine the sample seal to ensure that it is intact, temper proof and of acceptable quality.

h) **Packaging unit**
Examine the packaging size(s) declared in the application form to verify its sameness as packaging unit for the submitted samples and to find out if the applicant intends to produce other pack sizes apart from the submitted samples.

i) **Shelf life**
Examine the declared shelf life in the application form as justified by the submitted stability study report and its relevance to the manufacture and expiry dates declared on the product label.

j) **Product manufacturing process (flow chart)**
Examine to verify if the product manufacturing process flow assures the quality and safety of the final product.

k) **Authoritative Export permit**
Examine the export permit (and/or Phyto-sanitary certificate in case of a plant or herbal based food supplement) if it is authentic and issued by a competent food regulatory authority from the country of origin. The certificate shall show that the product is safe for human consumption and approved for use in that country.

l) **GMP and/or HACCP compliance certificate**
Scrutinize the certificate of GMP and/or HACCP complianceissued by competent authorities from the country of origin of the product.For locallymanufactured products, scrutinize premises inspection reports carried out by the Rwanda FDA. In addition to these Rwanda FDA shall conduct GMP inspection of manufacturing facility in the country of origin before registration.

m) **Certificates of analysis**
Examine the submitted certificate of laboratory analysis to verify the relevance of the tests performed before, during or after processing. For all tests, examine the criteria used for acceptance of the product. For characteristic ingredients such as nutrients, compare levels obtained from analysis with those declared on sample label and test results from the Rwanda FDA Laboratory.

Depending on the nature and characteristics of the dietary supplement, the following parameters may beanalysed for raw materials and/or finished products:

i) Identification of ingredients or marker(s);
ii) Purity or content of specific entity or marker compounds(s);
iii) Absence of adulterants;
iv) Known toxic, or undesirable components;

v) Insects or foreign organic matters;
vi) Organic volatile impurities;
vii) Pesticides;
viii) Fungcides (eg Quintozene) in ginseng;
ix) Mycotoxins;
x) Microbial enumeration tests such as total aerobic microbial count, Moulds & yeasts and Bile- tolerant gram negative bacteria;
xi) Viable specific microorganisms such as Salmonella species, Escherichia coli, Clostridium species and Staphylococcus aureus;
xii) Heavy metals;
xiii) Moisture content;
xiv) Loss on Drying;
xv) Ash (total, acid-soluble ash);
xvi) Residue on Ignition;
xvii) pH;
xviii) Disintegration;
xix) Dissolution;
xx) Weight variation;
xxi) Friability;

n) **Stability study report**
Critically examine the method used to determine the established product shelf life including:
i) Study design (protocol);
ii) Test conditions (humidity and temperature);
iii) Test intervals and duration;
iv) Type of container used (Testing should be conducted using containers and closures intended for marketing of products);
v) Parameters to be tested should be those susceptible to change and are likely to influence the quality and safety of the finished product.They shall at least cover appearance for product form, levels of characteristic ingredients, physicochemical properties (such as pH, dissolution, purity, disintegration) and microbial limits depending on the nature of the product; and
vi) Test results from item (v) above.

o) **Name and address of manufacturer**
Examine to confirm that name and address (physical and/or postal) of manufacturer declared in the application form matches with the one appearing on the sample label and all other submitted documents.

p) **Ingredients**
i) Examine the ingredients including additives declared in the application form and sample to ensure that they don't contradict each other.

ii) Examine if the characteristic ingredients are permissible for use in the manufacture of products intended for use as a dietary supplement.

iii) Examine the names of additives in the application form to ensure that they have been declared by their specific names or appropriate E numbers.

iv) Examine the proportions and purpose of use for each ingredient to ensure that they comply with specifications.

v) Pay special attention in examining food additives to establish that they are permissible; have been used to the right type ofdietary supplement and in accordance with the prescribed levels.

2.4 **Evaluation of labelling**

Labelling information on dietary supplement is another area requiring critical evaluation. The evaluator is required to evaluate the labelling information as follows:

a) Food Labelling Regulations,

b) Examine to verify the presence of clear and concise instruction for use in order to ensure correct utilization of the product. Instruction for use shall include dosage with respect to user age group and physiological condition;

c) Examine for presence of warning and cautionary statement associated with the use of the product. This may include the statements like '*Do not exceed the recommended daily dosage*' '*Keep out of reach of children*' '*contraindications*';

d) For products bearing claims on the label, examine if they comply with CODEX Guidelines for use of Nutrition and Health claims;

e) In case of products which contain genetically modified organisms/irradiated ingredient(s) examine to ensure that the fact is declared on the label;

f) Examine to ensure that pictorial presentation if present, is notmisleading the consumers; and

g) Examine any additional information which may be contained in the leaflet or the package insert to ensure that they comply with food labelling regulations.

2.4 **Request for Laboratory Analysis**

Hidden quality and safety attributes of food supplement cannot be observed without laboratory analysis. The evaluator is guided to consider the following in prescribing parameters for laboratory analysis:

a) Identify critical area with respect to safety and quality of the products that needs confirmation from laboratory analysis based on observations encountered during evaluation of the product;

b) Prescribe parameters for laboratory analysisas prescribed in guideline 2.3 (m) of these guidelines to ascertain the quality and safety of a product; and

c) Analysis of nutritional composition and other characteristic ingredientmay be requested to verify the levels declared on the label

CHAPTER 3

3.0 EVALUATION OF VITAMINS, MINERALS, AMINO ACIDS ANDESSENTIAL FATTY ACIDS DIETARY SUPPLEMENTS

3.1 Vitamins and Minerals

Vitamin and mineral food supplements are sources in concentrated forms of those nutrients alone or in combinations, marketed in forms such as capsules, tablets, powders, solutions, etc., that are designed to be taken in measured small-unit quantities, but are not in a conventional food form and whose purpose is to supplement the intake of vitamins and/or minerals from the normal diet.

3.1.1 Specific requirements

a) Examine to ensure that vitamin and mineral food supplements contain vitamins/provitamins and mineralswhose nutritional value for human beings has been proven by scientific data and whose status as vitamins and minerals is recognised by FAO and WHO;

b) Examine to ensure that sourcesof vitamins and minerals is either natural or synthetic substances as listed in **Annex1** and the purity criteria for such substances should take into account FAO/WHO standards.If FAO/WHO standards are not available, international Pharmacopoeias or recognized international standards may be used;

c) Examine to ensure that a minimum level of each nutrient per daily portion of consumption as suggested by the manufacturer is not less than 15% of the Recommended Daily Intake (RDI)levels as determined by FAO/WHO (Annex2); and

d) Examine to ensure that the levels of each vitamin and mineral per daily portion of consumption as recommended by the manufacturer donot exceed the Upper Safe Levels (USL) asprescribed in Annex 6.

3.2 Amino Acids Dietary Supplements

Amino acidfood supplements are the sources of Proteins in concentrated form. Amino acids can be classified into 2 classes as follows;

a) Essential amino acids are those which cannot be synthesized by humans and hence must be provided in the diet or supplemented. These include Histidine, Isoleucine, Leucine, Lysine, Methionine, Phenylalanine, Threonine, Tryptophan and Valine.

b) Nonessential amino acids are those which can be synthesized from other amino acids or from other precursors. These include Alanine, Aspartic acid, Asparagine, Glutamic acid, Glutamine, Serine, Arginine Cysteine Glycine Proline and Tyrosine.

3.2.1 **Specific Requirements**

a) Examine to ensure that a minimum level of amino acid contained in anamino acid food supplement per daily portion of consumption as suggested by the manufacturer shall be not less than 15% of the amino acid requirements as shown in **Annex3.**

b) Examine to ensure that sourcesof amino acids are either natural or synthetic substances as listed in **Annex 5.**

c) Scrutinize presence of the information listed below and evaluate their contents to ascertain if they guarantee the safety and quality of the product with reference to scientifically recognized international publications eg.EFSA, WHO/FAO

i) Summary of the amino acid supplement that describe the source, origin, purity and product formulation including concentration and/or amount of characteristic substance and excipient;

ii) Information on functional characterization studies conducted *In vitro* and *In vivo;*

iii) Information to demonstrate efficacy of the amino acid supplement in relation to the claimed nutritional and/or physiological function to human; and

iv) The data used to establish Recommended Intake or dosage and intended user.

3.3 **Essential Fatty Acids**

Essential fatty acids are fatty acidsrequired for biological processes but do not include the fats that only act as fuel and cannot be synthesized in the body. There are two categories of essential fatty acids supplements namely alpha-linolenic acid (classified as omega-3 fatty acid) and linoleic acid (classified as omega-6 fatty acid).

3.3.1 **Specific Requirements**

a) Examine to ensure that minimum level of essential fatty acids contained in essential fatty acids food supplement per daily portion of consumption as suggested by the manufacturer shall be not less than 15% of the amino acid requirements as shown in **Annex4.**

b) Scrutinize presence of the information listed below and evaluate their contents to ascertain if they guarantee the safety and quality of the product

with reference to scientifically recognized international publications eg.EFSA, WHO/FAO

i) Summary of the essential fatty acid supplement that describe the source, origin, purity and product formulation including concentration and/or amount of characteristic substance and excipient;
ii) Information on functional characterization studies conducted *In vitro* and *In vivo;*
iii) Information to demonstrate efficacy of the amino acid supplement in relation to the claimed nutritional and/or physiological function to human;
iv) The data used to establish Recommended Intake or dosage and intended user.

CHAPTER 4

4.0 EVALUATION OF THE SAFETY OF FOOD SUPPLEMENTS CONTAINING INGREDIENTS OTHER THAN NUTRIENTS

In addition to nutrients, other characteristic substances used in food supplements include plants, plant extracts, animal products and extracts, herbs, bee products and microbes. For each ingredient, evaluation should involve critical review of the following scientific information necessary to support safety of each ingredient.

4.1 Evaluation of Safety of Plants, Plant Extracts and Herbal based Dietary Supplement

Scrutinize presence of the information listed below and evaluate their contents to ascertain if they guarantee the safety and quality of the product with reference to scientifically recognized international publications eg. EFSA, WHO/FAO.

i) Summary of the plant(s) profile used including botanical name, genus, species, subspecies, plant parts used, whether cultivated or wild and treatment to obtain raw materials;

ii) Description of the nutritional and/physiological benefit of the herbal ingredient(s)/supplement to the intended user;

iii) Description of chemical constituent(s) or characteristic substance of the ingredient claimed to provide desired nutritional and/or physiological effect.

iv) Data to demonstrate the safety of the supplement in human beings in view of the following:-

a) Experimental data including *In vivo* and *In vitro* studies;

b) Data to demonstrate clinical studies in human, adverse events and justification for the recommended dosing;

c) Potential interactions with prescription drugs/or with other food supplements if any; and

d) Caution in relation to any undesired effects which may result from use of the product as dietary supplement.

4.2 Enzymes and other Metabolites Supplement

Scrutinize presence of the information listed below and evaluate their contents to ascertain if they guarantee the safety and quality of the product with reference to scientifically recognized international publications eg.EFSA, WHO/FAO

i) Information about the source (Plant, animal/microorganisms) of the enzyme/metabolite;

ii) Profile of the source from which enzyme/metabolite is derived including botanical/scientific name, genus, species, subspecies, parts from which enzymes/metabolites are extracted, extraction practices;

iii) Description of the physiological benefit of the enzyme/metabolite supplement to the intended user;
iv) Description of chemical constituent(s) or characteristic substance of the ingredient claimed to provide desired physiological effect;
v) Data to demonstrate the safety of the enzyme/metabolite in human beings in view of the following:-
   a) Data to demonstrate clinical studies in human, adverse events and justification for the recommended dosing;
   b) Experimental data including In vivo and In vitro studies;
   c) Potential interactions with prescription drugs/or with other dietary supplements if any; and
   d) Cautions in relation to any undesired effects which may result from the use of the enzyme/metabolite as a food supplement.

4.3 **Evaluation of ProbioticSupplements**

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host.

Scrutinize presence of the information listed below and evaluate their contents to ascertain if they guarantee the safety and quality of the product with reference to scientifically recognized international publications eg.EFSA, WHO/FAO:-

i) Strain identification by phenotypic and genotypic methods;
ii) Summary of the profile of the organism, including genus, species, strain;
iii) Information on functional characterization studies conducted *In vitro* and *In vivo;*
iv) Description of the physiological benefit of the probiotics to the intended user;
v) Data to demonstrate efficacy of the probiotics in relation to the claimed physiological function to human;
vi) Data to demonstrate the safety of the probiotics in view of the following:-
   a) Proof that the strain does not cause the following common side effects:-
      i) Systemic infections;
      ii) Deleterious metabolic activities;
      iii) Excessive immune stimulation in susceptible individuals; and
      iv) Gene transfer;
   b) Data to demonstrate recommended intake and intended user;
   c) Experimental data including *In vivo* and *In vitro* studies; and
   d) Potential interactions with prescription drugs/or with other dietary supplements if any.

4.4 **Evaluation of Prebiotics Supplements**

Prebiotics are non-digestible fiber compounds that pass undigested through the upper part of the gastrointestinal tract and stimulate the growth and/or activity of advantageous bacteria

that colonize the large bowel by acting as substrate for them. Basically prebiotics are food for probiotics.

Scrutinize presence of the information listed below and evaluate their contents to ascertain if they guarantee the safety and quality of the product with reference to scientifically recognized international publications eg.EFSA, WHO/FAO:-

i) Summary of the information on prebiotic that describe the source, origin, purity andproduct formulation including concentration and/or amount of characteristic substance and excipient;
ii) Information on functional characterization study conducted *In vitro* and *In vivo;*
iii) Information to demonstrate efficacy of the prebiotic in relation to the claimed physiological function to human;
iv) Data to demonstrate the safety of prebiotic based on *In vivo* and *In vitro* studies; and
v) The dataused to establish Recommended Intake or dosage and intended user.

4.5 **Evaluation of animal products and Animal extracts Supplements**

These are supplements derived from animal products and/or animal extracts like colostrum, adrenal extract, egg yolk andbee products.

Scrutinize presence of the information listed below and evaluate their contents to ascertain if they guarantee the safety and quality of the product with reference to scientifically recognized international publications eg.EFSA, WHO/FAO:-

i) Information on the source of the animal extract and/or animal product;
ii) Body part(s) or animal product from which extract(s) are obtained and extraction practices/methods;
iii) Proof that the extract is obtained from a healthy animal;
iv) Description of the nutritional and/physiological effect of the animal extract or product to the intended user;
v) Data to demonstrate the safety of the animal extract in human beings in view of the following:-
    a) Potential contaminants e.g chemical including veterinary drug residues and microbial contaminants;
    b) Data to demonstrate clinical studies in human, adverse events and justification for the recommended dosing;
    c) Experimental data including *In vivo* and *In vitro* studies;
    d) Potential Interactions with prescription drugs/or with other dietary supplements; and
    e) Cautions in relation to any undesired effects which may result from use of the animal extract or product as dietary supplement.

ANNEX 1: LIST OF VITAMIN AND MINERAL SUBSTANCES WHICH MAY BE USED IN THE MANUFACTURE OF FOOD SUPPLEMENTS

A. Vitamins

1. VITAMIN A
(a) Retinol
(b) Retinyl acetate
(c) Retinylpalmitate
(d) Beta-carotene

2. VITAMIN D
(a) Cholecalciferol
(b) Ergocalciferol

3. VITAMIN E
(a) D-alpha-tocopherol
(b) DL-alpha-tocopherol
(c) D-alpha-tocopheryl acetate
(d) DL-alpha-tocopheryl acetate
(e) D-alpha-tocopheryl acid succinate

4. VITAMIN K
(a) Phylloquinone (phytomenadione)

5. VITAMIN B1
(a) Thiamin hydrochloride
(b) Thiamin mononitrate

6. VITAMIN B2
(a) Riboflavin
(b) Riboflavin 5'-phosphate, sodium

7. NIACIN
(a) Nicotinic acid
(b) Nicotinamide

8. PANTOTHENIC ACID
(a) D-pantothenate, calcium
(b) D-pantothenate, sodium
(c) Dexpanthenol

9. VITAMIN B6

(a) Pyridoxine hydrochloride
(b) Pyridoxine 5'-phosphate

10. FOLIC ACID
(a) Pteroylmonoglutamic acid

11. VITAMIN B12
(a) Cyanocobalamin
(b) Hydroxocobalami

12. BIOTIN
(a) D-biotin

13. VITAMIN C
(a) L-ascorbic acid
(b) sodium-L-ascorbate
(c) calcium-L-ascorbate
(d) potassium-L-ascorbate
(e) L-ascorbyl 6-palmitate

B. Minerals
Calcium carbonate
Calcium chloride
Calcium salts of citric acid
Calcium gluconate
Calcium glycerophosphate
Calcium lactate
Calcium salts of orthophosphoric acid
Calcium hydroxide
Calcium oxide

Magnesium acetate
Magnesium carbonate
Magnesium chloride
Magnesium salts of citric acid
Magnesium gluconate
Magnesium glycerophosphate
Magnesium salts of orthophosphoric acid
Magnesium lactate
Magnesium hydroxide
Magnesium oxide
Magnesium sulphate

Ferrous carbonate
Ferrous citrate

Ferric ammonium citrate
Ferrous gluconate
Ferrous fumarate
Ferric sodium diphosphate
Ferrous lactate
Ferrous sulphate
Ferric diphosphate (ferric pyrophosphate)
Ferric saccharate
Elemental iron (carbonyl+electrolytic+hydrogen reduced)

Cupric carbonate
Cupric citrate
Cupric gluconate
Cupric sulphate
Copper lysine complex

Sodium iodide
Sodium iodate
Potassium iodide
Potassium iodate

Zinc acetate
Zinc chloride
Zinc citrate
Zinc gluconate
Zinc lactate
Zinc oxide
Zinc carbonate
Zinc sulphate

Manganese carbonate
Manganese chloride
Manganese citrate
Manganese gluconate
Manganese glycerophosphate
Manganese sulphate

Sodium bicarbonate
Sodium carbonate
Sodium chloride
Sodium citrate
Sodium gluconate
Sodium lactate
Sodium hydroxide
Sodium salts of orthophosphoric acid

Potassium bicarbonate
Potassium carbonate
Potassium chloride
Potassium citrate
Potassium gluconate
Potassium glycerophosphate
Potassium lactate
Potassium hydroxide
Potassium salts of orthophosphoric acid

Sodium selenate
Sodium hydrogen selenite
Sodium selenite

Chromium (III) chloride
Chromium (III) sulphate

Ammonium molybdate (molybdenum (VI))
Sodium molybdate (molybdenum (VI))

Potassium fluoride
Sodium fluoride

ANNEX 2: RECOMMENDED NUTRIENT INTAKES (RNI) FOR VARIOUS AGE GROUPS

Table 1: Vitamins

Group	Thiamine (Vit.B1) mg/day	Riboflavin (Vit. B2) mg/day	Niacin (Vit. B3) mg/day	Pantothenic acid (Vit. B5) mg/day	Pyridoxine (Vit. B6) mg/day	Folic acid (Vit. B9) mcg/day	Cynocobalamin(Vit. B12) mcg/day	Biotin mcg/day	Vitamin A mcg RE/day	Vitamin C mg/day	Vitamin D mcg/day	Vitamin E mg/day	Vitamin K mcg/day
Infants													
0-6 month	0.2	0.3	2	1.7	0.1	80	0.4	5.0	375	25	5	2.7	5
7-12 month	0.3	0.4	4	1.8	0.3	80	0.5	6.0	400	30	5	2.7	10
Children													
1-3 years	0.5	0.5	6	2.0	0.5	160	0.9	8.0	400	30	5	5	15
4-6 years	0.6	0.6	8	3.0	0.6	200	1.2	120	450	30	5	5	20
7-9 years	0.9	0.9	12	4.0	1.0	300	1.8	200	500	35	5	7	25
Adolescents													
Females 10-18 years	1.1	1.0	16	5.0	1.2	400	2.4	25.0	600	40	5	7.5	35-55
Males 10-18 years	1.2	1.3	16	5.0	1.3	400	2.4	25.0	600	40	5	10	35-55
Adults													
Females 19+ years	1.1	1.1	14	5.0	1.3 *(19-50yrs)* 1.5 *(>50yrs)*	400	2.4	30.0	500 *(19-65yrs)* 600 *(65+ yrs)*	45	5 *(19-50yrs)* 10 *(51-65yrs)* 15 *(65+yrs)*	7.5	55
Males 19+ years	1.2	1.3	16	5.0	1.3 1.7	400	2.4	30.0	600	45	5 *(19-50yrs)* 10 *(51-65yrs)*	10	65

											15 *(65+yrs)*		
Pregnancy	1.4	1.4	18	6.0	1.9	600	2.6	30.0	800	55	5	7.5	55
Lactation	1.5	1.6	17	7.0	2.0	500	2.8	35.0	850	70	5	7.5	55

Source: FAO/WHO

Table 2: Minerals

Age/group	Calcium (mg/day)	Copper (mg/day)	Iodine (mcg/day)	Iron (mg/day)	Magnesium (mg/day)	Potassium (mg/day)	Phosphorous (mg/day)	Selenium (mcg/day)	Zinc (mg/day)
Infants & children									
0-3 month	500	0.33-0.55	40	-		-	-	6	-
0-6 month									
Human milk fed					26				
Formula fed					36				
4-6 month	500	0.37-0.62	40	8.5		-		6	-
7-12 month	600	0.60	50	8.5	54	800	310	12	5.6
1-3 years	400	0.56	70-120	5.0	60	800	310	20	5.5
4-6 years	450	0.57	70-120	5.5	76	1100	350-450	24	6.5
7-10 years	500	0.75	70-120	9.5	100	2000	350-450	25	7.5
Males									
11-14 years	600-700	1.00	120-150	15.0	230	3100	775	36	12.1
15-18 years	500-600	1.33	120-150	9.0	230	3100	775	40	13.1
19+ years	400-500	1.35	120-150	9.0	260 *(19-65yrs)* 224 *(65+yrs)*	3100	540	40	9.4
Female									
11-14 years	600-700	1.00	120-150	16.0	220	3100	625	30	10.3
15-18 years	500-600	1.15	120-150	12.5	220	3100	625	30	10.2
19+ years	400-500	1.15	120-150	12.5 *(19-50yrs)* 9.5 *(50+yrs)*	220 *(19-65yrs)* 190 *(65+yrs)*	3100	540	30	6.5
Pregnancy	1000-1200	1.15	175	12.5	220	3100	540	39	7.3-13.3

Lactation	1000-1200	1.25	175	10.5	+50	3100	+400	42-46	12.7 *(0-4month)* 11.7 *(4+month)*

Source: FAO/WHO

Note: These are the recommended amounts that an individual needs to ingest per day.

ANNEX 3: ESSENTIAL AMINO ACID REQUIREMENTS FOR ADULTS

SN	AMINO ACID	Requirements in adults (mg/Kg body weight per day
1	Lysine	30
2	Leucine	39
3	Isoleucine	20
4	Valine	26
5	Threonine	15
6	Phenylalanine	25
7	Tyrosine	25
8	Tryptophan	4
9	Methionine	10.4
10	Cysteine	4.1
11	Histidine	10

Source:

WHO Technical Report Series 935

PROTEIN AND AMINO ACID REQUIREMENTS IN HUMAN NUTRITION

Report of a joint WHO/FAO/UNU Expert Consultation

ANNEX 4: ADEQUATE INTAKE OF ESSENTIAL FATTY ACIDS

(i) Adequate Intake (AI) for Omega-6 Fatty Acids

Life Stage	Age	Source	Males (g/day)	Females (g/day)
Infants	0-6 months	Omega-6 PUFA*	4.4	4.4
Infants	7-12 months	Omega-6 PUFA*	4.6	4.6
Children	1-3 years	LA#	7	7
Children	4-8 years	LA	10	10
Children	9-13 years	LA	12	10
Adolescents	14-18 years	LA	16	11
Adults	19-50 years	LA	17	12
Adults	51 years and older	LA	14	11
Pregnancy	all ages	LA	-	13
Breast-feeding	all ages	LA	-	13

*The various omega-6 polyunsaturated fatty acids (PUFA) present in human milk can contribute to the AI for infants. # LA, linoleic acid

(ii). Adequate Intake (AI) for Omega-3 Fatty Acids (1)

Life Stage	Age	Source	Males (g/day)	Females (g/day)
Infants	0-6 months	ALA, EPA, DHA*	0.5	0.5
Infants	7-12 months	ALA, EPA, DHA	0.5	0.5
Children	1-3 years	ALA	0.7	0.7
Children	4-8 years	ALA	0.9	0.9
Children	9-13 years	ALA	1.2	1.0
Adolescents	14-18 years	ALA	1.6	1.1
Adults	19 years and older	ALA	1.6	1.1
Pregnancy	all ages	ALA	-	1.4
Breast-feeding	all ages	ALA	-	1.3

*All omega-3 polyunsaturated fatty acids present in human milk can contribute to the AI for infants. ALA, α-linolenic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

Source: The Food and Nutrition Board of the US Institute of Medicine

ANNEX 5: ADVISORY LIST OF AMINO ACIDS AND OTHER NUTRIENTS FOR USE IN FOOD SUPPLEMENTS

Abbreviations:

BP	=	British Pharmacopoeia
BPC	=	British Pharmaceutical Codex
DAB	=	Deutsches Arzneibuch
DAC	=	Deutscher Arzneimittel-Codex
DVFA	=	Danish Veterinary and Food Administration
FCC	=	Food Chemicals Codex
FSANZ	=	Food Standards Australia New Zealand
FU	=	Farmacopoea Ufficiale della Republica Italiana
JP	=	The Pharmacopeia of Japan
Jap Food Stan	=	Japanese Food Standard
MI	=	Merck Index
MP	=	Martindale Pharmacopoeia
ÖAB	=	Österreichisches Arzneibuch
Ph Eur	=	Pharmacopoeia Europaea
Ph Franç	=	Pharmacopée Française
Ph Helv	=	Pharmacopoeia Helvetica
Ph Int	=	International Pharmacopoeia
USP	=	The United States Pharmacopoeia

S/N	Nutrient Source	Purity requirements
	1. Amino acids	
1.	L-Arginine	FCC, USP, Ph Eur, BP, DAB
2.	L-Arginine-hydrochloride	FCC, USP, Ph Eur, BP, DAB
3.	L-Cystine	FCC, USP, Ph Eur
4.	L-Cystine dihydrochloride	MI
5.	L-Cysteine	DAB
6.	L-Cysteine hydrochloride	FCC, Ph Eur
7.	L- Histidine	FCC, USP, Ph Eur, DAB
8.	L- Histidine hydrochloride	FCC, Ph Eur, DAB
9.	L-Isoleucine	FCC, USP, Ph Eur, DAB
10.	L-Isoleucine hydrochloride	FCC, USP
11.	L-Leucine	FCC, USP, Ph Eur, DAB
12.	L-Leucine hydrochloride	MI, FCC, USP
13.	L-Lysine	USP
14.	L-Lysine monohydrochloride	FCC, USP, Ph Eur, DAB
15.	L-Methionine	Ph Int, FCC, USP, Ph Eur, DAB
16.	L-Phenylalanine	FCC, USP, Ph Eur DAB
17.	L-Tryptophan	FCC, USP, Ph Eur, DAB
18.	L-Tyrosine	FCC, USP, Ph Eur, DAB
19.	L-Valine	FCC, USP, Ph Eur, DAB
20.	L-Alanine	FCC, USP, Ph Eur, DAB
21.	L-Arginine-L- aspartate	Ph Eur
22.	L-Aspartic acid	FCC, USP, Ph Eur
23.	L -Citrulline	USP, DAC
24.	L- Glutamic acid	JECFA(1987), FCC, USP, Ph Eur
25.	L-Glutamine	FCC, USP, DAB
26.	Glycine	FCC, USP, Ph Eur
27.	L-Ornithine	MI, FCC
28.	L-Ornithine monohydrochloride	DAB
29.	L-Proline	FCC, USP, Ph Eur, DAB
30.	L-Serine	USP, Ph Eur, DAB
31.	N-Acetyl-L- cysteine	USP, Ph Eur, DAB
32.	N-Acetyl-L- methionine	FCC
33.	L-Lysine acetate	FCC, USP, MP; Ph Eur
34.	L-Lysine L- Aspartate	Jap Food, Stan
35.	L-Lysine L- glutamate	Jap Food, Stan

	dihydrate	
36.	Magnesium L- aspartate	Ph Eur
37.	Calcium L- glutamate	JECFA, FCC, Jap Food Stan
38.	Potassium L- glutamate	JECFA, FCC, Jap Food Stan
	2. Carnitine	
39.	L-Carnitine	FCC, USP, Ph Eur
40.	L-Carnitine hydrochloride	FCC
41.	L-Carnitine tartrate	FCC, Ph Eur
	Taurine	
42.	Taurine	USP, JP
	Choline	
43.	Choline	FCC, USP
44.	Choline chloride	FCC, DAC, DAB
45.	Choline citrate	NF
46.	Choline hydrogen tartrate	DAB
47.		FCC, NF, DAB
48.	Choline bitartrate	FCC, NF, DAB
	Inositols	
49.	Myo-Inositol (=meso-Inositol)	FCC, DAC
50.	**Nucleotides**	
51.	Adenosine 5- mono-phosphate(AMP)	FSANZ
52.	Cytidine 5- mono-phosphate(CMP)	FSANZ, Jap Food Stan
53.	Guanosine 5- mono-phosphate(GMP)	JECFA (1985)
54.	Inosine 5- monophos- phate (IMP)	JECFA (1974)
55.	Disodium Uridine 5-monophosphate salt	FSANZ, Jap Food Stan
56.	Disodium Guanosine 5-monophosphate salt	FCC, JECFA, FSANZ, Jap Food Stan
57.	Disodium Inosine 5-monophosphate salt	FCC, JECFA, FSANZ, Jap Food Stan

Source:

Advisory list of Amino acids and other nutrients for use in foods for special dietary uses intended for infants and young children (CAC/GL 10-1979)

ANNEX 6: DIETARY REFERENCE INTAKES (DRIS): TOLERABLE UPPER INTAKE LEVELS, VITAMINS

Food and Nutrition Board, Institute of Medicine, National Academies

Life Stage Group	Vitamin A (µg/d)[a]	Vitamin C (mg/d)	Vitamin D (□g/d)	Vitamin E (mg/d)[b,c]	Vitamin K (mg/d)	Thia-Min (mg/d)	Ribo-Flavin (mg/d)	Niacin (mg/d)[c]	Vitamin B_6 (mg/d)	Folate (□g/d)[c]	Vitamin B12 (mg/d)	Panto-thenic Acid (mg/d)	Bio-Tin (□g/d)	Cho-line (g/d)	Carote-noids[d]
Infants															
0 to 6 mo	600	ND[e]	25	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
6 to 12 mo	600	ND	38	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Children															
1□3 y	600	400	63	200	ND	ND	ND	10	30	300	ND	ND	ND	1.0	ND
4□8 y	900	650	75	300	ND	ND	ND	15	40	400	ND	ND	ND	1.0	ND
Males															
9□13 y	1,700	1,200	100	600	ND	ND	ND	20	60	600	ND	ND	ND	2.0	ND
14□18 y	2,800	1,800	100	800	ND	ND	ND	30	80	800	ND	ND	ND	3.0	ND
19□30 y	3,000	2,000	100	1,000	10	100	200	35	100	1,000	2000	200	900	3.5	ND
31□50 y	3,000	2,000	100	1,000	10	100	200	35	100	1,000	2000	200	900	3.5	ND
51□70 y	3,000	2,000	100	1,000	ND	ND	ND	35	100	1,000	ND	ND	ND	3.5	ND
> 70 y	3,000	2,000	100	1,000	ND	ND	ND	35	100	1,000	ND	ND	ND	3.5	ND
Females															
9□13 y	1,700	1,200	100	600	ND	ND	ND	20	60	600	ND	ND	ND	2.0	ND
14□18 y	2,800	1,800	100	800	ND	ND	ND	30	80	800	ND	ND	ND	3.0	ND
19□30 y	3,000	2,000	100	1,000	10	100	200	35	100	1,000	2000	200	900	3.5	ND
31□50 y	3,000	2,000	100	1,000	10	100	200	35	100	1,000	2000	200	900	3.5	ND
51□70 y	3,000	2,000	100	1,000	ND	ND	ND	35	100	1,000	ND	ND	ND	3.5	ND

> 70 y	3,000	2,000	100	1,000	ND	ND	ND	35	100	1,000	ND	ND	ND	3.5	ND
Pregnancy															
14□18 y	2,800	1,800	100	800	ND	ND	ND	30	80	800	ND	ND	ND	3.0	ND
19□30 y	3,000	2,000	100	1,000	ND	ND	ND	35	100	1,000	ND	ND	ND	3.5	ND
31□50 y	3,000	2,000	100	1,000	ND	ND	ND	35	100	1,000	ND	ND	ND	3.5	ND
Lactation															
14□18 y	2,800	1,800	100	800	ND	ND	ND	30	80	800	ND	ND	ND	3.0	ND
19□30 y	3,000	2,000	100	1,000	ND	ND	ND	35	100	1,000	ND	ND	ND	3.5	ND
31□50 y	3,000	2,000	100	1,000	ND	ND	ND	35	100	1,000	ND	ND	ND	3.5	ND

NOTE: A Tolerable Upper Intake Level (UL) is the highest level of daily nutrient intake that is likely to pose no risk of adverse health effects to almost all individuals in the general population. Unless otherwise specified, the UL represents total intake from food, water, and supplements. Due to a lack of suitable data, ULs could not be established for vitamin K, thiamin, riboflavin, vitamin B_{12}, pantothenic acid, biotin, and carotenoids. In the absence of a UL, extra caution may be warranted in consuming levels above recommended intakes. Members of the general population should be advised not to routinely exceed the UL. The UL is not meant to apply to individuals who are treated with the nutrient under medical supervision or to individuals with predisposing conditions that modify their sensitivity to the nutrient.

[a] As preformed vitamin A only.

[b] As □-tocopherol; applies to any form of supplemental □-tocopherol.

[c] The ULs for vitamin E, niacin, and folate apply to synthetic forms obtained from supplements, fortified foods, or a combination of the two. [d] □-Carotene supplements are advised only to serve as a provitamin A source for individuals at risk of vitamin A deficiency.

[e] ND = Not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts. Source of intake should be from food only to prevent high levels of intake

Source: Dietary Reference Intakes for Calcium,,phosphorus,Magnesium,Vitamin D,and fluoride(1997);Dietary Reference Intakes for Thiamin,Riboflavin,Niacin,Vitamin B_6, Folate,Vitamin B_{12}, Pantothenic Acid ,Biotin and Choline (1998); Dietary Reference intake for Vitamin C,Vitamin E,Selenium and Carotenoids(2000);Dietary Reference Intake for Vitamin A,Vitamin K,Arsenic,Boron,Chromium,Copper,Iodine,Iron,Manganese,Molybdenum,Nickel,Silicon,Vanadium and Zinc(2001);and Dietary Reference Intake for Calcium and Vitamin D(2011).These reports may be accessed via www.nap.ed

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