

GOOD MANUFACTURING PRACTICES (GMP's)
FOR DIETARY SUPPLEMENTS

1. Definitions

In addition to definitions included in applicable legislation, the following definitions shall also apply:

- (a) **"Acceptance criteria"** means the product specifications and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with an associated sampling plan, that are necessary for making a decision to accept or reject a lot or batch (or any other convenient subgroups of manufactured units).
- (b) **"Adequate"** means that which is needed to accomplish the intended purpose in keeping with good public health practice.
- (c) **"Batch or Lot"** means a specific quantity of a finished product or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.
- (d) **"Composition"** means, as appropriate:
- (1) the identity of a dietary ingredient or dietary supplement, and
 - (2) the concentration of a dietary ingredient (e.g., weight or other unit of use/weight or volume), or the potency or activity of one or more dietary ingredients, as indicated by appropriate procedures.
- (e) **"Dietary ingredient"** means an ingredient intended for use or used in a dietary supplement that is:
- (1) a vitamin,
 - (2) a mineral,
 - (3) an herb or other botanical,
 - (4) an amino acid,
 - (5) a microorganism for human consumption
 - (6) a dietary substance for use by man to supplement the diet by increasing the total dietary intake,
 - (7) a nutrient or other substance with a nutritional or physiological function, or
 - (8) a concentrate, metabolite, constituent, extract, or combination of any of the foregoing ingredients.
- (f) **"Dietary product"** means either a dietary ingredient or a dietary supplement as defined in this part.
- (g) **"Dietary supplement"** means a product marketed under food law, containing one or more dietary ingredients in a concentrated form, which may also contain other ingredients, presented in a form intended for single or multiple dose administration, including but not limited to tablets, capsules, powders or liquids.
- (h) **"In-process material"** means any material fabricated, compounded, blended, ground, extracted, sifted, sterilized, derived by chemical reaction or processed in any other way that is produced for, and used in, the preparation of a dietary product.

(i) "**Lot**" means "batch" as defined in this part.

(j) "**Lot number**" means any distinctive combination of letters, numbers, or symbols, or any combination of them from which the complete history of the manufacture, processing, packing, holding, and distribution of a batch or lot of a finished dietary ingredient, dietary supplement or other material can be determined.

(k) "**Manufacture**" or "**manufacturing**" includes all operations associated with the production of dietary products, including ingredient processing and handling, pre-blending, product fabrication, packaging and labeling operations, testing, and quality control, and post-production distribution and management, of a dietary ingredient or dietary supplement.

(l) "**Microorganisms**" means yeasts, molds, bacteria, and viruses and includes, but is not limited to, species having public health significance. The term "undesirable microorganisms" includes those microorganisms that are of public health significance, that subject a dietary product to accelerated decomposition, that indicate that a dietary ingredient or dietary supplement is contaminated with filth, or that otherwise may cause a dietary product to be adulterated. Occasionally in these regulations, the adjective "microbial" is used instead of an adjectival phrase containing the word microorganism.

(m) "**Quality assurance**" means the sum total of the organized arrangements made with the object of ensuring that the final products are of the quality required for their intended use.

(n) "**Quality control operation**" means a planned and systematic procedure for taking all actions necessary to prevent a dietary product from being adulterated.

(o) "**Quality control unit**" means any person or organizational element designated by the firm to be responsible for the duties relating to quality control operations.

(p) "**Raw material**" means any ingredient intended for use in the manufacture of a dietary ingredient or dietary supplement, including those that may not appear in such finished product.

(q) "**Representative**" sample means a sample that consists of a number of units that are drawn based on rational criteria, such as random sampling, and is intended to assure that the sample accurately portrays the material being sampled.

(r) "**Rework**" means clean, unadulterated material that has been removed from processing for reasons other than insanitary conditions or that has been successfully reconditioned by reprocessing and that is suitable for use in the manufacture of a dietary product.

(s) "**Shall**" is used to state mandatory requirements.

(t) "**Should**" is used to state recommended or advisory practices.

2. Food GMP Compliance

In addition to the requirements stated below, all applicable *food* GMP standards, including those related to (i) qualifications and hygienic practices related to personnel; and (ii) the design, construction, maintenance and sanitation of buildings, facilities, equipment, utensils, dietary products and other ingredients, shall be followed in the manufacturing of dietary supplements.

3. Hazard Analysis and Critical Control Points (HACCP)

Where applicable, and required by governing regulation(s), the principles of Hazard Analysis and Critical Control Points (HACCP) shall be observed in the manufacturing of dietary supplements. This shall include the identification of any step in their activities which is critical to ensuring food safety and ensure that adequate safety procedures are identified, implemented, maintained and reviewed in accordance with the following HACCP principles:

- analysing the potential food hazards in a food business operation,
- identifying the points in those operations where food hazards may occur,
- deciding which of the points identified are critical to food safety - the 'critical points',
- identifying and implementing effective control and monitoring procedures at those critical points, and
- reviewing the analysis of food hazards, the critical control points and the control and monitoring procedures periodically and whenever the food business operations change.

4. Quality Assurance, Quality Control and Laboratory Operations

Appropriate quality control operations and/or Quality Assurance activities shall be employed to assure that dietary products conform to appropriate standards of purity, quality, composition and claimed label content, and that packaging materials are safe and suitable for their intended purpose.

(a) Quality Control Unit.

There shall be a quality control unit, which has a staff that shall be qualified by training or experience and shall receive appropriate dietary supplement GMP training.

(1) The quality control unit shall have the responsibility and authority to:

- (i) Approve or reject all procedures, specifications, controls, tests and examinations, or deviations from them, that impact the purity, quality, composition and claimed label content of a dietary ingredient or dietary supplement; and
- (ii) Approve or reject all raw materials, packaging materials, labeling, and finished dietary products, including products manufactured, processed, packed, or held under contract by another company, based on adequate determination of conformance to established specifications; and
- (iii) Assure that completed production records are reviewed as appropriate. Quality control shall be responsible for evaluation of errors committed in the manufacture of a product and shall have the final authority to determine if the error may be corrected in such manner that the product can be approved for distribution or must be destroyed. Such evaluations and their resolution must be documented and maintained with and/or cross-referenced in the batch production record.

(2) Adequate in house or contracted laboratory facilities shall be available, as needed, to the quality control unit.

(3) The responsibilities and procedures applicable to the quality control unit shall be established in writing and followed.

(b) Laboratory records.

Laboratory records shall be maintained and shall include complete data derived from all specified tests.

(c) “Best Before”/Expiration dating.

(1) Whenever a dietary ingredient or dietary supplement bears a “best before” or an expiration date, such date shall be supported by data and rationale to reasonably assure that the product meets established specifications at the indicated date.

(2) For the initial determination of shelf life, appropriate stability studies, including accelerated studies and data from similar product formulation(s), should be used in the absence of sufficient real time studies. Product shelf life shall be confirmed and may be extended on the basis of real time studies on dietary products stored under labeled storage conditions.

(d) Self - Inspections.

Self inspections should be conducted at intervals, according to a pre-arranged program by designated competent person(s) from the company, in order to monitor the implementation and compliance with Good Manufacturing Practice principles and to propose necessary corrective measures which, with a statement of actions subsequently taken, shall be recorded in writing.

5. Production and Process Controls

(a) Master production and control records.

To assure uniformity from batch to batch, a master production and control record shall be prepared for the manufacture of each dietary ingredient and dietary supplement, and shall be reviewed and approved by the quality control unit.

(b) Batch production and control records.

(1) Individual batch production and control records shall be prepared and followed for each batch of dietary product produced and shall include complete information relating to the production and control of each batch. These records shall be an accurate reproduction of the appropriate master production and control record and shall include documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished.:

(2) Any deviation from written, approved specifications, standards, test procedures or other laboratory control mechanisms shall be recorded and justified.

(c) Handling, storage and testing of raw materials, in-process materials and rework.

(1) Raw materials, in-process materials and rework shall be inspected and segregated, quarantined or otherwise handled as necessary to ascertain that they are clean and suitable for processing into dietary products and shall be stored under conditions that will protect against adulteration and minimize deterioration. Containers of raw materials should be inspected on receipt to assure that their condition has not contributed to the adulteration or deterioration of the contents. Liquid or dry raw materials and other ingredients received and stored in bulk form shall be held in a manner that protects against contamination.

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(2) Raw agricultural materials that contain soil or other contaminants shall be washed or cleaned as necessary. Water used for washing, rinsing, or conveying raw agricultural materials shall be safe and of adequate sanitary quality. Notwithstanding the general requirement for potable water, water may be reused for washing, rinsing, or conveying raw agricultural materials if it does not increase the level of contamination of such materials.

(3) Raw materials, in-process materials and rework shall be held in bulk, or in containers designed and constructed so as to protect against adulteration and shall be held at such temperature and relative humidity and in such a manner as to prevent a dietary ingredient or dietary supplement from becoming adulterated. Material scheduled for rework shall be identified as such.

(4) Frozen raw materials and other ingredients shall be kept frozen. If thawing is required prior to use, it shall be done in a manner that prevents the raw materials and other ingredients from becoming adulterated.

(5) Written procedures shall be established and followed describing the receipt, identification, examination, handling, sampling, testing and approval or rejection of raw materials.

(6) Each lot of raw material shall be identified with a distinctive lot number and shall be appropriately controlled according to its status (e.g. quarantined, approved, rejected).

(7) Raw material samples shall be examined and tested where appropriate to confirm their identity, freedom from adulteration, microbiological contamination (where appropriate) and their conformance with other specifications and applicable regulations. Proof of such conformance may be satisfied by a certificate of analysis from the supplier, with the exception that each lot of raw material shall undergo at least one test by the manufacturer to verify its identity.

(8) Approved raw materials shall be rotated so that the oldest approved stock is used first. Deviation from this requirement is permitted if such deviation is temporary and appropriate, and approved in writing by the Quality Control Unit.

(9) Raw materials shall be retested or re-examined and approved or rejected by the quality control unit after the specified shelf-life in storage or after exposure to air, heat, or other conditions that are likely to adversely affect the purity, quality, composition or claimed label content of the raw material.

(10) Rejected raw materials, shall be identified, and controlled under a system that prevents their use in manufacturing or processing operations for which they are unsuitable.

(d) Manufacturing operations.

(1) All operations in the receiving, inspecting, transporting, segregating, preparing, manufacturing, packaging, and storing of dietary products shall be conducted under such conditions and controls as are necessary to minimize the potential for the growth of micro-organisms, or for the adulteration, degradation or contamination of raw materials, in-process materials and finished products.

(2) Chemical, microbial, or extraneous-material testing procedures shall be used where necessary to identify sanitation failures or possible product adulteration. All product that has become contaminated to the extent that it is adulterated shall be rejected, or if permissible, treated or processed to eliminate the contamination.

(3) Measures such as sterilizing, irradiating, pasteurizing, freezing, refrigerating, controlling pH or controlling water activity (a_w) that are taken to destroy or prevent the growth of undesirable microorganisms, particularly those of public health significance, shall be adequate under the conditions of manufacture, handling, and distribution to prevent dietary products from being adulterated.

(4) All raw material containers, compounding and storage containers, processing lines and major equipment used during the production of a batch shall be properly identified at all times to indicate their contents and when necessary, the processing phase of the batch.

(5) Written procedures shall be established and followed that describe appropriate tests, and/or examinations to be conducted, and related acceptance criteria that may be necessary to assure the purity, quality, composition and claimed label content of the finished product.

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- (6) Written procedures shall be established and followed prescribing the method for reprocessing raw materials, in-process materials, or finished goods batches that do not conform to finished goods standards or specifications. Finished goods manufactured using such materials shall meet all purity, quality, composition and claimed label content standards.
- (7) Mechanical manufacturing steps such as cutting, sorting, inspecting, shredding, drying, grinding, blending and sifting shall be performed so as to protect dietary ingredients and dietary supplements against adulteration. Compliance with this requirement may be accomplished by providing adequate physical protection of dietary products from contact with adulterants. Protection may be provided by adequate cleaning and sanitizing of all processing equipment between each manufacturing step.
- (8) To assure batch uniformity and integrity of dietary products, written procedures shall be established and followed that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch.

(e) Packaging and labeling operations.

- (1) Filling, assembling, packaging, and other operations shall be performed in such a way that dietary products are protected against adulteration.
- (2) Written procedures should be established and followed describing in sufficient detail the control procedures employed for the receipt, storage, handling, sampling, examination, and/or testing that may be necessary to assure the identity of labeling and the appropriate identity, cleanliness and quality characteristics of packaging materials for dietary products and for the clearance of lines between different products.
- (3) For dietary supplements, labels and other labeling materials for each different product type, strength, or quantity of contents should be stored separately with suitable identification.
- (4) Obsolete or non-compliant labels, labeling, and other packaging materials for dietary products shall be destroyed.
- (5) Written procedures shall be established and followed to assure that correct labels, labeling, and packaging materials are issued and used for dietary products.
- (6) Dietary ingredient and dietary supplement packages shall be identified with a lot number that permits determination of the history of the manufacture and control of the batch.
- (7) Packaged and labeled dietary supplements shall be examined to provide assurance that containers and packages in the lot have the correct label, 'Best Before', 'Use By' or expiry dating, and lot number. The quality control unit shall reject products not meeting specifications.

6. Warehousing, Distribution and Post-Distribution Procedures

(a) Storage and distribution.

- (1) Storage and transportation of finished product shall be under conditions that will protect product against physical, chemical, and microbial adulteration as well as against deterioration of the product and the container. The conveying vehicle must, where necessary, be designed and constructed to permit adequate cleaning
- (2) Adequate distribution records shall be maintained and retained by the manufacturer at least one year beyond expected product shelf life, or designated "best before" or expiration date, whereby an effective product recall can be achieved should one become necessary.
- (3) An effective recall procedure should be written and practiced.

(b) Reserve samples.

An appropriately identified reserve sample that is representative of each batch of a dietary product should be retained and stored under conditions consistent with the product labeling until at least one year after the “best before” or expiration date, or if no such date is identified on the product, for at least three years after the date of manufacture. The reserve sample should be stored in the same immediate container-closure system in which the finished product is marketed or in one that provides similar protection. The reserve sample shall consist of at least twice the quantity necessary to perform all appropriate tests.

(c) Records retention.

- (1) Any laboratory, production, control or distribution record specifically associated with a batch of product shall be retained for at least one year after the “best before” or expiration date of the batch, or if no such date is identified on the product, for at least three years after the date of manufacture.
- (2) Raw material records shall be maintained for at least one year after the “best before” or expiration date of the last batch of product incorporating the raw material, or if no such date is identified on the product, for at least three years after the date of manufacture of the finished product.

(d) Complaint files.

- (1) Written procedures describing the handling of all written and oral complaints regarding a dietary product shall be established and followed. Such procedures shall include provisions for review by the quality control unit of any complaint involving the possible failure of a product to meet any of its specifications and, for such products, a determination as to the need for an investigation.
- (2) A written record of each complaint shall be maintained, until at least 1 year after the “best before” or expiration date of the product, or 1 year after the date that the complaint was received, whichever is longer.
- (3) The written record shall include, where known: the name and description of the product, lot number, “best before” or expiration date, name of complainant, nature of complaint, and reply to complainant, if any.
- (4) Where an investigation is conducted, the written record shall include the findings of the investigation and follow-up action taken.

(e) Returned products.

Returned dietary products shall be identified as such and held. If the conditions under which returned dietary products have been held, stored, or shipped before or during their return, or if the condition of the product, its container, carton, or labeling as a result of storage or shipping, casts doubt on the purity, quality, composition or claimed label content of the product, the returned product shall be destroyed unless examination, testing or other investigations prove the product meets appropriate standards of purity, quality, composition and claimed label content. If the tamper-evident seal of a returned product is broken, it should be destroyed and not reprocessed. A product may be reprocessed provided the subsequent product meets appropriate specifications. Records pertaining to returned products that are subsequently reprocessed and/or redistributed shall be maintained and shall include the name and description of the product, lot number, reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned product.

(f) Product salvaging.

Dietary products that have been subjected to improper storage conditions including extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace. Whenever there is a question whether products have been subjected to such conditions, salvaging operations may be conducted only if there is (a) evidence from laboratory tests that the products meet all applicable standards of purity, quality, composition and claimed label content, and (b) evidence from inspection of the premises that the products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident. Records including name, lot number, and disposition shall be maintained for products subject to this section.

7. Contract Manufacturing

Whenever a contract manufacturer performs any portion of product manufacturing, the responsibilities of the contract manufacturer concerning the accomplishment of GMP functions shall be documented.