(6) A statement of theoretical yield of a manufactured dietary ingredient or dietary supplement expected at each point, step, or stage of the manufacturing process where control is needed to prevent adulteration, and the expected yield when you finish manufacturing the dietary ingredient or dietary supplement, including the maximum and minimum percentages of theoretical yield beyond which a deviation investigation of a batch is performed and material review is conducted and disposition decision is made;

(7) A description of packaging and a copy of the label to be used; and

(8) Written instructions including, but not limited to, the following:

(i) Specifications for each point, step, or stage in manufacturing the dietary ingredient or dietary supplement necessary to prevent adulteration;

(ii) Sampling and testing procedures;

(iii) Specific actions necessary to perform and verify points, steps, or stages, necessary to meet specifications and otherwise prevent adulteration, including, but not limited to, one person weighing or measuring a component and another person verifying the weight or measure and one person adding the component and another person verifying the addition;

(iv) Special notations and precautions to be followed; and

(v) Corrective action plans for use when a specification is not met.

(c) You must have the quality control unit review and approve each master manufacturing record and any modifications to a master manufacturing record.

(d) You must keep master manufacturing records in accordance with § 111.125.

§ 111.50 What requirements apply to establishing a batch production record?

(a) You must prepare a batch production record every time you manufacture a batch of a dietary ingredient or dietary supplement and the batch production record must include complete information relating to the production and control of each batch.

(b) Your batch production record must accurately follow the appropriate master manufacturing record and you must perform each step in producing the batch.

(c) The batch production record must include, but is not limited to, the following information:

(1) The batch, lot, or control number;

(2) Documentation at the time of performance, showing the date on which each step of the master manufacturing record was performed, and the initials of the persons performing each step;

(3) The identity of equipment and processing lines used in producing the batch;

(4) The date and time of the maintenance, cleaning, and sanitizing of the equipment and processing lines used in producing the batch;

(5) The shipment lot unique identifier of each component, dietary ingredient, dietary supplement, packaging, and label used;

(6) The identity and weight or measure of each component used;

(7) The initials of the person responsible for weighing or measuring each component used in the batch and the initials of the person verifying the weight or measure;

(8) The initials of the person responsible for adding the components to the batch and the initials of the person verifying the addition;

(9) A statement of the actual yield and a statement of the percentage of theoretical yield at appropriate phases of processing;

(10) The actual test results for any testing performed during the batch production;

(11) Documentation that the dietary ingredient and dietary supplement meets specifications;

(12) Copies of all container labels used and the results of examinations conducted during the label operation to ensure that the containers have the correct label;

(13) Any documented material review and disposition decision; and

(14) Signature of the quality control unit to document batch production record review and any approval for reprocessing or repackaging,

(d) The quality control unit must review the batch production record established in paragraph (c) of this section.

(1) If a batch deviates from the master manufacturing record, including any deviation from specifications, the quality control unit must conduct a material review and make a disposition decision and record any decision in the batch production record.

(2) The quality control unit must not approve and release for distribution any batch of dietary ingredient or dietary supplement that does not meet all specifications.

(e) The quality control unit must document the review performed in accordance with paragraph (d) of this section and it must be documented at the time of performance. The review and documentation must include, but is not limited to, the following:

(1) Review of component, dietary ingredient, and dietary supplement receiving records including review of testing and examination results;

(2) Identification of any deviation from the master manufacturing record that may have caused a batch or any of its

components to fail to meet specifications identified in the master production record;

(3) Records of investigations, conclusions, and corrective actions performed in accordance with paragraph (d) of this section; and

(4) The identity of the person qualified by training and experience who performed the investigation in accordance with paragraph (d) of this section.

(f) You must not reprocess a batch that deviates from the master manufacturing record unless approved by the quality control unit. You must not reprocess a dietary ingredient or dietary supplement if it is rejected because of contamination with microorganisms of public health significance or other contaminants, such as heavy metals;

(g) Any batch of dietary ingredient or dietary supplement that is reprocessed must meet all specifications for the batch of dietary ingredient or dietary supplement and be evaluated and approved by the quality control unit before releasing for distribution. The results of the reevaluation by the quality control unit must be documented in the batch production record; and

(h) You must collect representative reserve samples of each batch of dietary ingredient or dietary supplement and keep the reserve samples for 3 years from the date of manufacture for use

in appropriate investigations including, but not limited to, consumer complaint investigations to determine whether, for example, the dietary ingredient or dietary supplement associated with a consumer complaint failed to meet any of its specifications for identity, purity, quality, strength, and composition.

(i) You must keep batch production records in accordance with § 111.125.

§ 111.60 What requirements apply to laboratory operations?

(a) You must use adequate laboratory facilities to perform whatever testing and examinations are necessary to determine that components, dietary ingredients, and dietary supplements received meet specifications; that specifications are met during in-process, as specified in the master manufacturing record; and that dietary ingredients and dietary supplements manufactured meet specifications.

(b)(1) You must establish and follow laboratory control processes that are approved by the quality control unit. Laboratory control processes must include, but are not limited to, the following:

(i) Use of criteria for selecting appropriate examination and testing methods;

(ii) Use of criteria for establishing appropriate specifications; and

(iii) Use of sampling plans for obtaining representative samples of:

(A) Components, dietary ingredients, and dietary supplements received to determine whether specifications are met;

(B) In-process materials during the batch manufacturing when testing or examination is required in the master manufacturing record;

(C) Each batch of dietary ingredient or dietary supplement manufactured to determine that the dietary ingredient or dietary supplement meets specifications;

(D) Packaging and labels received to determine that the materials meet specifications; and

(E) Each batch of packaged and labeled dietary ingredients or dietary supplements to ensure that the label specified in the master manufacturing record has been applied.

(iv) Use of criteria for selecting standard reference materials used in performing tests and examinations;

(v) Use of appropriate test method validations; and

(vi) Use of test methods and examinations in accordance with established criteria.

(2) The person who conducts the testing and examination at the time of performance, must document that laboratory methodology established in accordance with this section is followed. The documentation must include the testing and

examination results.

(3) You must keep laboratory examination and testing records in accordance with § 111.125.

(c) You must verify that the laboratory examination and testing methodologies are appropriate for their intended use.

(d) You must identify and use the appropriate validated testing method for each established specification for which testing is required to determine whether the specification is met.

§ 111.65 What requirements apply to manufacturing operations?

(a) You must design or select manufacturing processes to ensure that dietary ingredient or dietary supplement specifications are consistently achieved.

(b) You must conduct all manufacturing operations in accordance with adequate sanitation principles.

(c) You must take all the necessary precautions during the manufacture of a dietary ingredient or dietary supplement to prevent contamination of components, dietary ingredients, or dietary supplements. These precautions include, but are not limited to:

(1) Performing manufacturing operations under conditions and controls that protect against the potential for growth of microorganisms and the potential for contamination;

(2) Washing or cleaning components that contain soil or

other contaminants;

(3) Using water that meets the National Primary Drinking Water regulations or, where necessary, higher sanitary quality and that complies with all applicable Federal, State, and local regulations for water that is used in the manufacturing operation. If you reuse water that was used to wash components to remove soil or contaminants, the reused water must be safe and of adequate sanitary quality so that it does not become a source of contamination;

(4) Performing chemical, microbiological, or other testing, as necessary to prevent the use of contaminated components, dietary ingredients, and dietary supplements;

(5) Sterilizing, pasteurizing, freezing, refrigerating, controlling hydrogen-ion concentration (pH), controlling humidity, controlling water activity (a_w), or using any other effective means to remove, destroy, or prevent the growth of microorganisms and prevent decomposition;

(6) Holding components, dietary ingredients, and dietary supplements that can support the rapid growth of microorganisms of public health significance in a manner that prevents the components, dietary ingredients, and dietary supplements from becoming adulterated;

(7) Identifying and holding any components, dietary ingredients, or dietary supplements, for which a material review

and disposition decision is required, in a manner that protects the components, dietary ingredients, or dietary supplements against contamination and mixups;

(8) Performing mechanical manufacturing steps (such as cutting, sorting, inspecting, shredding, drying, grinding, blending, and sifting) by any effective means to protect the dietary ingredients or dietary supplements against contamination. Such steps must include consideration of:

(i) Cleaning and sanitizing contact surfaces;

(ii) Using temperature controls; and

(iii) Using time controls.

(9) Using effective measures to protect against the inclusion of metal or other foreign material in components, dietary ingredients, or dietary supplements. Compliance with this requirement must include consideration of the use of:

(i) Filters or strainers;

(ii) Traps;

(iii) Magnets; or

(iv) Electronic metal detectors.

(10) Segregating and identifying all containers for a specific batch of dietary ingredients or dietary supplements to identify their contents and, where necessary, the phase of manufacturing; and

(11) Identifying all processing lines and major equipment

used during manufacturing to indicate their contents including the name of the dietary ingredient or dietary supplement and the specific batch or lot number and, when necessary, the phase of manufacturing.

(d) You must conduct a material review and make a disposition decision in accordance with § 111.35(i) for any component, dietary ingredient, or dietary supplement that fails to meet specifications or that is or may be adulterated. If the material review and disposition decision allows you to reprocess the component, dietary ingredient, or dietary supplement, you must retest or reexamine the component, dietary ingredient, or dietary supplement to ensure that it meets specifications and is approved by the quality control unit.

(e)(1) The person who performs the material review and disposition decision in accordance with this section must document at the time of performance the results of the material review and disposition decision and such documentation must be maintained with the batch production record.

(2) The documentation must include, but not be limited to:

(i) The date and time the requirement was performed; and

(ii) The signature of the person who performed the requirement.

(3) You must keep manufacturing operation records in accordance with § 111.125.

§ 111.70 What requirements apply to packaging and label operations?

(a) You must take necessary actions to ensure that each packaging container for holding dietary ingredients or dietary supplements meets specifications so that the condition of the packaging container will not contaminate your dietary ingredients or dietary supplements nor cause them to deteriorate;

(b) You must fill, assemble, package, and perform other related operations in a way that protects your dietary ingredients or dietary supplements against adulteration and misbranding. You must do this using any effective means, including but not limited to, the following:

(1) Cleaning and sanitizing all filling and packaging equipment, utensils, and dietary ingredient or dietary supplement containers, as appropriate;

(2) Protecting manufactured dietary ingredients and dietary supplements from contamination, particularly airborne contamination;

(3) Using sanitary handling procedures;

(4) Establishing physical or spatial separation of packaging and labels from operations on other dietary ingredients and dietary supplements to prevent mixups;

(5) Identifying, by any effective means, filled dietary ingredient or dietary supplement containers that are set aside

and held in unlabeled condition for future label operations, to prevent mixups;

(6) Identifying the dietary ingredient or dietary supplement with a batch, lot, or control number that can be used to determine the manufacturing history and control of the batch;

(7) Examining a representative sample of each batch of the packaged and labeled dietary ingredient or dietary supplement to ensure that the dietary ingredient or dietary supplement meets specifications and that the label specified in the master manufacturing record has been applied; and

(8) Suitably disposing of labels and other packaging for dietary ingredients or dietary supplements that are obsolete or incorrect to ensure that they are not used in any future packaging and label operations.

(c) You must conduct a material review and make a disposition decision of any packaged and labeled dietary ingredients or dietary supplements that do not meet specifications.

(d) You must only repackage or relabel dietary ingredients or dietary supplements after the quality control unit has approved and documented such repackaging or relabeling.

(e) You must retest or reexamine any repackaged or relabeled dietary ingredients or dietary supplements. They must meet all specifications and the quality control unit must approve

or reject their release for distribution.

(f)(1) You must control the issuance and use of packaging and labels and reconciliation of any issuance and use discrepancies; and

(2) You must examine, before packaging operations, packaging and labels for each batch of dietary ingredient or dietary supplement to ensure that the label and packaging conform to the master manufacturing record.

(g) The person that performs the requirements of this section must document at the time of performance that the requirements are performed including, but not limited to, documentation in the batch production record of:

(1) The identity and quantity of the packaging and labels used and reconciliation of any discrepancies between issuance and use;

(2) The examination conducted in accordance with paragraph (b)(7) of this section;

(3) The conclusions you reached from retests conducted in accordance with paragraph (e) of this section; and

(4) Any material reviews and disposition decisions for packaging and labels.

(h) You must keep packaging and label operations records required under this section in accordance with § 111.125.

§ 111.74 What requirements apply to rejected components, dietary

ingredients, dietary supplements, packaging, and labels?

You must clearly identify, hold, and control under a quarantine system any component, dietary ingredient, dietary supplement, packaging, and label that is rejected and unsuitable for use in manufacturing, packaging, or label operations.

9. Add subpart F to part 111 to read as follows:

Subpart F--Holding and Distributing

111.80 What requirements apply to holding components, dietary ingredients, dietary supplements, packaging, and labels?

111.82 What requirements apply to holding in-process material?

111.83 What requirements apply to holding reserve samples of components, dietary ingredients, and dietary supplements?

111.85 What requirements apply to returned dietary ingredients or dietary supplements?

111.90 What requirements apply to distributing dietary ingredients or dietary supplements?

Subpart F--Holding and Distributing

§ 111.80 What requirements apply to holding components, dietary ingredients, dietary supplements, packaging, and labels?

(a) You must hold components, dietary ingredients, and

dietary supplements under appropriate conditions of temperature, humidity, and light so that the identity, purity, quality, strength, and composition of the components, dietary ingredients, and dietary supplements are not affected.

(b) You must hold packaging and labels under appropriate conditions of temperature, humidity, and light so that the quality of the packaging and labels are not affected.

(c) You must hold components, dietary ingredients, dietary supplements, packaging, and labels under conditions that do not lead to the mixup, contamination, or deterioration of components, dietary ingredients, dietary supplements, packaging, and labels.

§ 111.82 What requirements apply to holding in-process material?

(a) You must identify and hold in-process material under conditions that will protect them against mixup, contamination, and deterioration.

(b) You must hold in-process material under appropriate conditions of temperature, humidity, and light.

§ 111.83 What requirements apply to holding reserve samples of components, dietary ingredients, and dietary supplements?

(a) For any reserve samples of components or dietary ingredients you collect, you must hold such reserve samples in a manner that protects against contamination and deterioration.

(b) You must hold reserve samples of dietary supplements in a manner that protects against contamination and deterioration. This includes, but is not limited to:

(1) Holding the reserve samples under conditions of use recommended or suggested in the label of the dietary supplement and, if no conditions of use are recommended or suggested in the label, then under ordinary conditions of use; and

(2) Using the same container-closure system in which the dietary supplement is marketed or in one that provides the same level of protection against contamination or deterioration.

§ 111.85 What requirements apply to returned dietary ingredients or dietary supplements?

(a) You must identify and quarantine returned dietary ingredients or dietary supplements until the quality control unit conducts a material review and makes a disposition decision.

(b) You must not salvage returned dietary ingredients and dietary supplements, unless:

(1) Evidence from their packaging (or, if possible, an inspection of the premises where the dietary ingredients and dietary supplements were held) indicates that the dietary ingredients and dietary supplements were not subjected to improper storage conditions; and

(2) Tests demonstrate that the dietary ingredients or dietary supplements meet all specifications for identity, purity, quality, strength, and composition.

(c) You must destroy or suitably dispose of the returned dietary ingredients or dietary supplements if such dietary ingredients or dietary supplements do not meet specifications for identity, purity, quality, strength, and composition, unless the quality control unit conducts a material review and makes a disposition decision to allow reprocessing.

(d) If the reason for a dietary ingredient or a dietary supplement being returned implicates associated batches, you must conduct an investigation of your manufacturing processes and those other batches to determine compliance with specifications.

(e) You must establish and keep records for this section on the material review and disposition decision and any testing conducted to determine compliance with established specifications in the master manufacturing record for the type of dietary ingredient or dietary supplement that was returned.

(f) You must keep returned dietary ingredient and dietary supplement records in accordance with § 111.125.

§ 111.90 What requirements apply to distributing dietary ingredients or dietary supplements?

Distribution of dietary ingredients and dietary supplements must be under conditions that will protect the dietary ingredients and dietary supplements against contamination and deterioration.

10. Add subpart G to part 111 to read as follows:

Subpart G--Consumer Complaints

§ 111.95 What requirements apply to consumer complaints?

(a) You must keep a written record of each consumer complaint.

(b) A qualified person must review all consumer complaints to determine whether the consumer complaint involves a possible failure of a dietary ingredient or dietary supplement to meet any of its specifications, or any other requirements of this part, including those specifications and other requirements that, if not met, may result in a possible risk of illness or injury.

(c) Your quality control unit must review all consumer complaints involving the possible failure of a dietary ingredient or dietary supplement to meet any of its specifications, or any other requirements of this part, including those specifications and other requirements that, if not met, may result in a possible risk of illness or injury, to determine whether there is a need to investigate the consumer complaint.

(d) Your quality control unit must investigate a consumer complaint when there is a reasonable possibility of a relationship between the quality of a dietary supplement and an adverse event.

(e) Your quality control unit's investigation of a consumer complaint must include the batch records associated with the dietary ingredient or dietary supplement involved in the consumer complaint. Your quality control unit must extend the investigation to other batches of dietary ingredients or dietary supplements that may have been associated with an adverse event.

(f) You must make and keep a written record of every consumer complaint that is related to good manufacturing practices. For the purposes of this regulation, a consumer complaint about product quality may or may not include concerns about a possible hazard to health. However, a consumer complaint does not include an adverse event, illness, or injury related to the safety of a particular dietary ingredient independent of whether the product is produced under good manufacturing practices. The consumer complaint written record must include, but is not limited to, the following:

(1) The name and description of the dietary ingredient or dietary supplement;

(2) The batch or lot number of the dietary supplement, if

available;

(3) The name of the complainant, if available;

(4) The nature of the complaint including how the consumer used the product;

(5) The reply to the complainant, if any; and

(6) Findings of the investigation and followup action taken when an investigation is performed.

(g)(1) The person who performs the requirements in accordance with this section must document at the time of performance that the requirement was performed.

(2) You must keep consumer complaint records in accordance with § 111.125.

11. Add subpart H to part 111 to read as follows:

Subpart H--Records and Recordkeeping

§ 111.125 What requirements apply to recordkeeping?

(a) You must keep written records required by this part for 3 years beyond the date of manufacture of the last batch of dietary ingredients or dietary supplements associated with those records.

(b) Records required under this part must be kept as

original records, as true copies (such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records), or as electronic records. If you use reduction techniques, such as microfilming, you must make suitable reader and photocopying equipment readily available to FDA. All electronic records must comply with part 11 of this chapter.

(c) You must have all records required under this part, or copies of such records, readily available during the retention period for authorized inspection and copying by FDA when requested.

12. Part 112 is added to read as follows:

PART 112--RESTRICTIONS FOR SUBSTANCES USED IN DIETARY SUPPLEMENTS

Subpart A--General Provisions [Reserved]

Subpart B--New Dietary Ingredients [Reserved]

Subpart C--Restricted Dietary Ingredients [Reserved]

Authority: 21 U.S.C. 321, 342, 343, 371.

Date:_____

_____

Lester M. Crawford,

Deputy Commissioner

Date:_____

_____

Tommy G. Thompson

Secretary of Health and Human Services